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Summary

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WO009319749	45	45	0	1
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L1 STR

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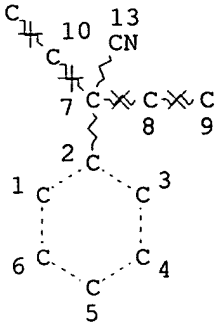

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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE
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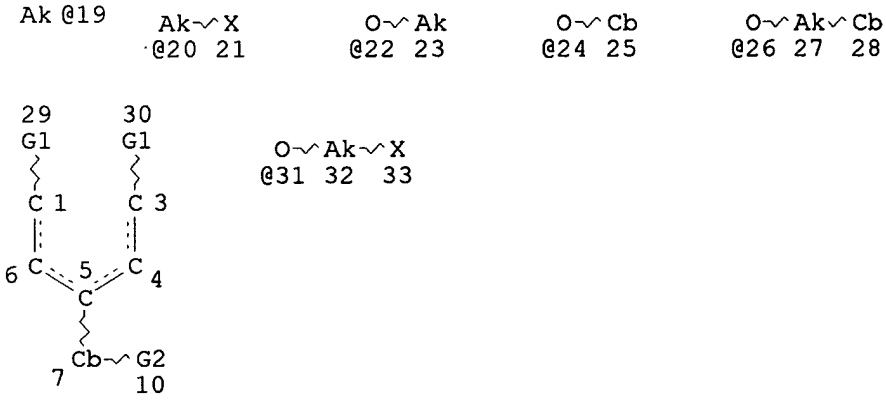

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GRAPH ATTRIBUTES:
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STEREO ATTRIBUTES: NONE
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L17 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

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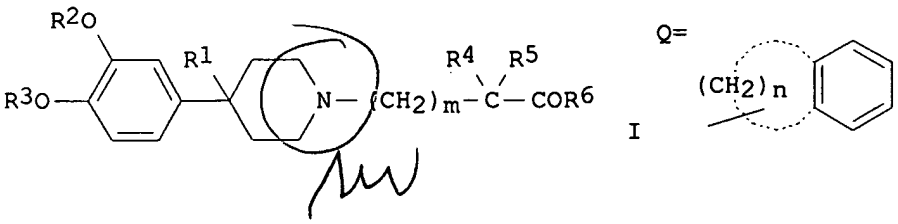
L17 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:142675 HCAPLUS
DOCUMENT NUMBER: 136:200104
TITLE: Preparation of 4-(3,4-dihydroxyphenyl)piperidine diethers derivatives as inhibitors of phosphodiesterase 4 (PDE4) and drugs containing these derivatives as the active ingredient
INVENTOR(S): Nakai, Hisao; Kishikawa, Katsuya
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014280	A1	20020221	WO 2001-JP6861	20010809
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001077738	A5	20020225	AU 2001-77738	20010809

PRIORITY APPLN. INFO.:
JP 2000-243881 A 20000811
JP 2000-357517 A 20001124
JP 2000-2000243881A 20000811
JP 2000-2000357517A 20001124
WO 2001-JP6861 W 20010809

OTHER SOURCE(S): MARPAT 136:200104
GI



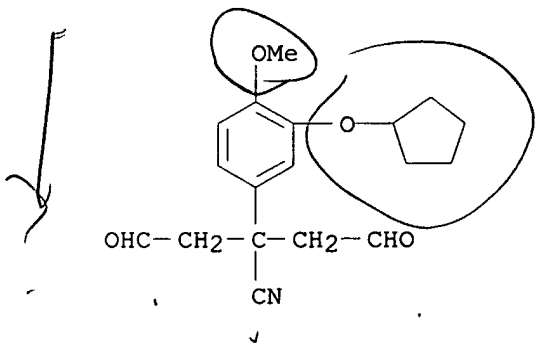
I

AB The title compds. [I; R1 = H, cyano; R2, R3 = H, C1-8 alkyl, C3-7 cycloalkyl, C3-7-cycloalkyl-C1-8 alkyl, C1-8 alkyl substituted by 1-3 halogen atoms, phenyl-C1-8 alkyl, C1-8 alkoxy-C1-8 alkyl, Q (where n = 1-5); R4,R5 = H, C1-8 alkyl or CR4R5 represents a satd. C3-7 carbocyclic ring; R6 = OH, C1-8 alkoxy, NHOH, Ph-C1-8 alkoxy; m = an integer of 1-4] or nontoxic salts thereof are prepd. Because of having a PDE4 inhibitory activity, the compds. I are useful in preventing and/or treating inflammatory diseases (asthma, obstructive pulmonary diseases, septicemia, sarcoidosis, nephritis, hepatitis, or enteritis), diabetic diseases, allergic diseases (allergic rhinitis, allergic conjunctivitis, or atopic dermatitis), autoimmune diseases (ulcerative colitis, Crohn's disease, rheumatism, psoriasis, multiple sclerosis, or collagen disease), osteoporosis, bone fracture, obesity, depression, Parkinson's disease, dementia, ischemic reperfusion disorder, leukemia, or AIDS. Thus, a mixt. of 239 mg 2-[4-(3-cyclopentyloxy-4-methoxyphenyl)-4-cyanopiperidin-1-yl]acetic acid, 192 mg 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, 4 mL DMF, and 0.35 mL (1-methoxy-1-methylethyl)oxyamine was stirred at room temp. for 3 h to give 289 mg N-(1-methoxy-1-methylethoxy)-2-[4-(3-cyclopentyloxy-4-methoxyphenyl)-4-cyanopiperidin-1-yl]acetamide which (280 mg) was stirred with a mixt. of 3 mL MeOH and 0.35 mL 2 N HCl at room temp. for 1 h to give 189 mg N-hydroxy-2-[4-(3-cyclopentyloxy-4-methoxyphenyl)-4-cyanopiperidin-1-yl]acetamide hydrochloride (II). II showed IC50 of 0.03 nM against human PDE4 from human monocyte U937 cell. A tablet and an ampule formulation contg. II were described.

IT **401518-83-0P**, 2-(3-Cyclopentyloxy-4-methoxyphenyl)-4-oxo-2-(2-oxoethyl)butanenitrile
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 4-(3,4-dihydroxyphenyl)piperidine diethers derivs. as inhibitors of phosphodiesterase 4 (PDE4) for therapeutic agents)

RN 401518-83-0 HCAPLUS

CN Benzeneacetonitrile, 3-(cyclopentyloxy)-4-methoxy-.alpha.,.alpha.-bis(2-oxoethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:896499 HCAPLUS
DOCUMENT NUMBER: 136:20072
TITLE: 1-Benzoyl-3-[2-[4-(1H-benzimidazole-2-carbonyl)piperidin-1-yl]ethyl]-3-phenylpyrrolidine derivatives and analogs as histamine and tachykinin receptor antagonists useful for the treatment of

allergic diseases

INVENTOR(S): Burkholder, Timothy P.; Bratton, Larry D.; Kudlacz, Elizabeth M.; Maynard, George P.; Kane, John M.; Santiago, Braulio

PATENT ASSIGNEE(S): Aventis Pharmaceuticals, Inc., USA

SOURCE: U.S., 77 pp., Cont.-in-part of U.S. Ser. No. 501,914, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

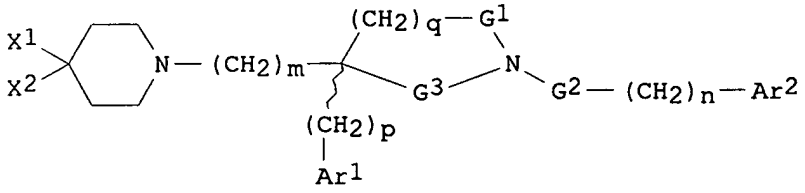
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6329392	B1	20011211	US 1998-79924	19980515
CA 2198084	AA	19960229	CA 1995-2198084	19950817
CN 1158612	A	19970903	CN 1995-195283	19950817
CN 1067385	B	20010620		
HU 76644	A2	19971028	HU 1997-1257	19950817
AT 177095	E	19990315	AT 1995-931551	19950817
ES 2132709	T3	19990816	ES 1995-931551	19950817
ZA 9507033	A	19960416	ZA 1995-7033	19950822
IL 115040	A1	20000229	IL 1995-115040	19950823
TW 430663	B	20010421	TW 1995-84108797	19950823

PRIORITY APPLN. INFO.: US 1994-295960 B2 19940825
US 1995-501914 B2 19950713

OTHER SOURCE(S): MARPAT 136:20072

GI



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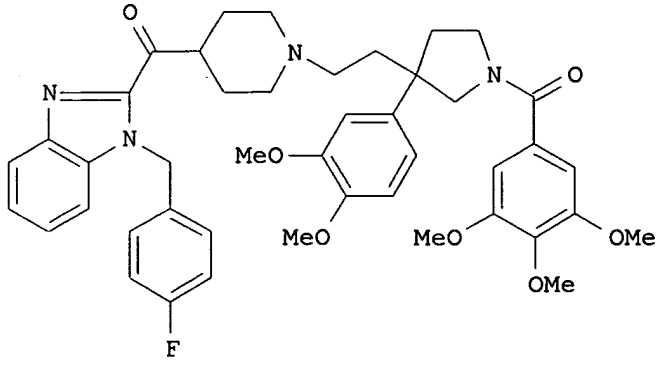


II

AB The present invention relates to novel substituted piperidine derivs. I

wherein: G1 is CH2 or CO; G2 is CH2 or CO; G3 is CH2 or CO; m is 2 or 3; n is 0 or 1; q is 1 or 2; p is 0 or 1; Ar1 = (un)substituted Ph, naphthyl, pyridyl, thienyl; Ar2 = (un)substituted Ph, pyridyl; X1 and X2 are defined in one of (A), (B), or (C): (A) X1 = H and X2 = substituted benzothiazole-2-carbonyl, diphenylmethyl, benzimidazolyl-2-carbonyl; (B) X1 = OH and X2 = substituted benzothiazol-2-yl, benzimidazol-2-yl; (C) X2 = (R5C6H4)C(Z1)(C6H4R6) wherein R5, R6 = from 1 to 3 substituents chosen independently from, e.g., H, halo, CF3, and X1 and Z1 taken together form a second bond between the carbon atoms bearing X1 and Z1; provided than when G1 is CO, then G2 and G3 are CH2, and that when G2 is CO, then G1 and G3 are CH2, and that when G3 is CO, then G1 and G2 are CH2; stereoisomers thereof, and pharmaceutically acceptable salts thereof which are useful as histamine receptor antagonists and tachykinin receptor antagonists. Such antagonists are useful in the treatment of allergic diseases including: seasonal rhinitis, allergic rhinitis, and sinusitis. Thus, e.g., substitution reaction of 4-[1-(4-fluorobenzyl)-1H-benzimidazole-2-carbonyl]piperidine with 1-(3,4,5-trimethoxybenzoyl)-3-(3,4-dimethoxyphenyl)-3-(2-methanesulfonyloxyethyl)pyrrolidine (prepn. given) afforded II which exhibited H1 receptor antagonism in vitro with pA2 = 7.50, and NK1 receptor binding affinity with IC50 = 31 nM.

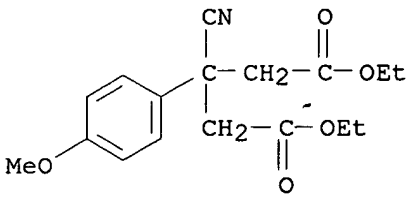
IT **40877-86-9P 40878-20-4P 167263-64-1P 178370-76-8P 178372-09-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(1-benzoyl-3-[2-[4-(1H-benzimidazole-2-carbonyl)piperidin-1-yl]ethyl]-3-phenylpyrrolidine derivs. and analogs as histamine and tachykinin receptor antagonists useful for the treatment of allergic diseases)

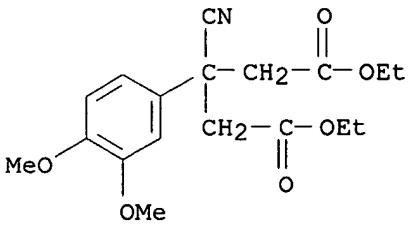
RN 40877-86-9 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



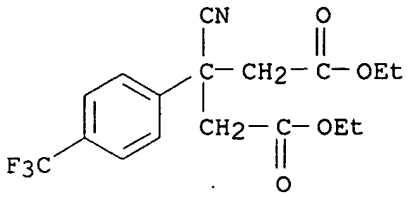
RN 40878-20-4 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)

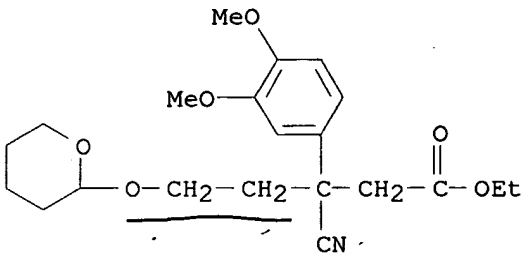


RN 167263-64-1 HCAPLUS

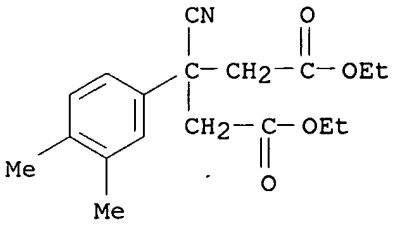
CN Pentanedioic acid, 3-cyano-3-[4-(trifluoromethyl)phenyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 178370-76-8 HCAPLUS
CN Benzenepropanoic acid, .beta.-cyano-3,4-dimethoxy-.beta.-[2-[(tetrahydro-2H-pyran-2-yl)oxy]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 178372-09-3 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethylphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:781460 HCAPLUS
DOCUMENT NUMBER: 135:344508
TITLE: Preparation of substituted benzimidazolyl[1,4]diazepanes useful as histamine and tachykinin receptor antagonists
INVENTOR(S): Maynard, George D.; Le, Tieu-binh
PATENT ASSIGNEE(S): Maynard, George, USA
SOURCE: U.S. Pat. Appl. Publ., 122 pp., Cont.-in-part of U.S. 6,194,406.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001034343	A1	20011025	US 2000-739741	20001218
US 6423704	B2	20020723		
US 6194406	B1	20010227	US 1997-513847	19971029

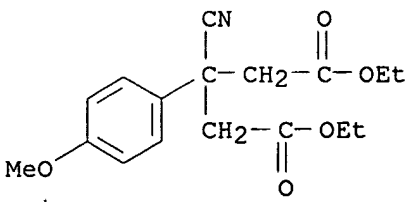
PRIORITY APPLN. INFO.: US 1995-70907P P 19951220
US 1996-736411 B2 19961024
US 1997-513847 A2 19971029
OTHER SOURCE(S): MARPAT 135:344508
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

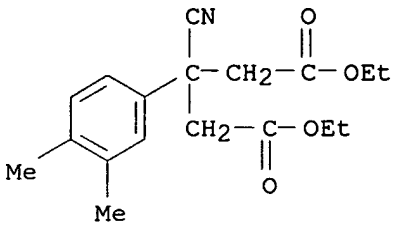
AB Title compds. I [m = 1 - 2; p = 0 - 1; G = CO, COCH2, SO2; R30 = alkyl, vinyl, alkyl-oxy-alkyl-cyclopropyl, alkylheterocyclyl; R33 = H, alkoxy, heterocyclyl, sulfonyloxy, etc.; R31-32 = H, alkoxy] were prepd. Over 100 synthetic examples were provided. E.g., 3,4-dimethoxyacetonitrile was alkylated twice with Et bromoacetate (THF, NaHMDS, dry-ice/acetone bath) and converted to 5-oxopyrrolidin-3-yl deriv. II (CoCl2.bul.6H2O, MeOH, 20.degree.C). II was converted to the pyrrolidine-alc. (THF, LAH, reflux, 18 h), N-acylated (CH2Cl2, NMM, 5.degree.C, 3,4,5-(MeO)3C6H2COCl), converted to the mesylate (CH2Cl2, MsCl, Et3N, < 2.degree.C - room temp. 18 h) and coupled to 4-(1-(2-ethoxyethyl)-1H-benzimidazol-2-yl)[1,4]diazepane (prepn. given, i-Pr2NEt, CH3CN, NaI, reflux, 3 days) to give example compd. III. I are histamine and tachykinin receptor antagonists (no data). Such antagonists are useful in the treatment of allergic rhinitis, inflammatory bowel diseases, Crohn's disease, ulcerative colitis, etc.

IT **40877-86-9P**, 3-Cyano-3-(4-methoxyphenyl)pentanedioic acid diethyl ester **178372-09-3P**, 3-Cyano-3-(3,4-dimethylphenyl)pentanedioic Acid Diethyl Ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of substituted benzimidazolyl[1,4]diazepanes useful as histamine and tachykinin receptor antagonists)

RN 40877-86-9 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



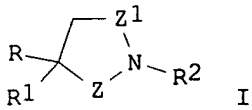
RN 178372-09-3 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethylphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:240149 HCAPLUS
DOCUMENT NUMBER: 134:266309
TITLE: Preparation of 4-(2-benzimidazolylamino)piperidines as histamine and tachykinin receptor antagonists
INVENTOR(S): Kane, John M.; Maynard, George D.; Burkholder, Timothy P.; Bratton, Larry D.; Dalton, Christopher R.; Santiago, Braulio; Kudlacz, Elizabeth M.
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Inc., USA
SOURCE: U.S., 106 pp., Cont.-in-part of U.S. Ser. No. 734,508, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6211199	B1	20010403	US 1997-513846	19971215
PRIORITY APPLN. INFO.:			US 1995-34609P P	19951117
			US 1996-734508 B2	19961017

OTHER SOURCE(S): MARPAT 134:266309
GI



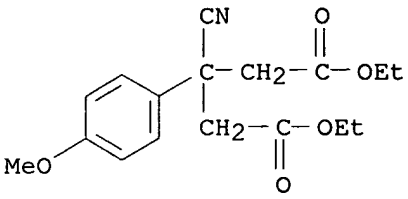
I

AB Title compds., e.g., I [R = R4Z4(CH2)m; R1 = (un)substituted Ph, -pyridinyl, -thienyl, etc.; R2 = (un)substituted (alkylenedioxy) benzyl, -benzoyl, etc.; R4 = e.g., (un)substituted 2-benzimidazolylamino; Z,Z1 = CH2 or CO; Z4 = piperidine-4,1-diyl; m = 2 or 3] were prepd. as histamine and tachykinin receptor antagonists (no data). Thus, 4-[1-(2-furylmethyl)-2-benzimidazolylamino]piperidine was condensed with 2-[1-[2-methoxy-5-(1-tetrazolyl)benzoyl]-3-phenyl-3-pyrrolidinyl]ethyl methanesulfonate (prepn each given) to give I [R = R4Z4CH2CH2, R1 = Ph, R2 = 2-methoxy-5-(1-

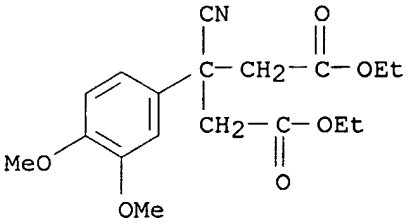
tetrazolyl)benzoyl, R4 = 1-(2-furylmethyl)-2-benzimidazolylamino, Z = Z1 = CH2, Z4 = piperidine-4,1-diyl].

IT **40877-86-9P 40878-20-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of (benzimidazolylamino)piperidines as antiallergics)

RN 40877-86-9 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 40878-20-4 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



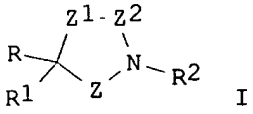
REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:149048 HCAPLUS
DOCUMENT NUMBER: 134:193454
TITLE: Preparation of N-(2-benzimidazolyl)-1,4-diazepanes as histamine and tachykinin receptor antagonists
INVENTOR(S): Kane, John M.; Maynard, George D.; Burkholder, Timothy P.; Bratton, Larry D.; Dalton, Christopher R.; Kudlacz, Elizabeth M.; Santiago, Braulio
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Inc., USA
SOURCE: U.S., 108 pp., Cont.-in-part of U.S. Ser. No. 736,411.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 6194406	B1	20010227	US 1997-513847		19971029
US 2001034343	A1	20011025	US 2000-739741		20001218
US 6423704	B2	20020723			
PRIORITY APPLN. INFO.:			US 1995-70907P	P	19951220
			US 1996-736411	B2	19961024
			US 1997-513847	A2	19971029

OTHER SOURCE(S): MARPAT 134:193454
GI

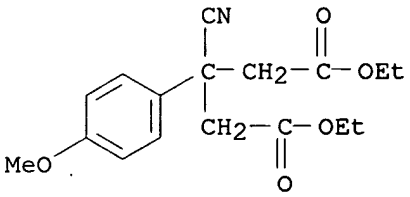


I

AB Title compds. [I; R = R5Z5Z4(CH2)m; R1 = (CH2)rR4; R2 = Z3(CH2)nR3; R3 = (un)substituted Ph, -1,3-benzodioxol-5-yl, -1,4-benodioxan-6-yl; R4 = (un)substituted Ph, -naphthyl, pyridinyl, -thienyl; R5 = H, (oxa)alkyl, (hetero)arylalkyl, etc.; Z,Z2 = CH2 or CO; Z1 = CH2 or CH2CH2; Z3 = CH2, CHMe, CO; Z4 = 1,4-diazepan-1,4-diyl; Z5 = (un)substituted benzimidazole-1,2-diyl; m = 2 or 3; n,r = 0 or 1] were prepd. as histamine and tachykinin receptor antagonists (no data). Thus, e.g., I [R = 2-[4-[1-(2-ethoxyethyl)benzimidazol-2-yl][1,4]diazepan-1-yl]ethyl, R1 = 3,4-(MeO)2C6H3, R2 = COC6H2(OMe)3-3,4,5, Z = Z1 = Z2 = CH2] was prepd.

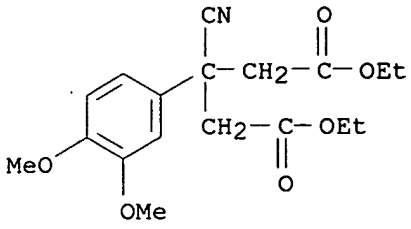
IT **40877-86-9P 40878-20-4P**, 3-Cyano-3-(3,4-dimethoxyphenyl)pentanedioic acid diethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of benzimidazolyldiazepanes as antiallergics and antiinflammatories)

RN 40877-86-9 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 40878-20-4 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)

6

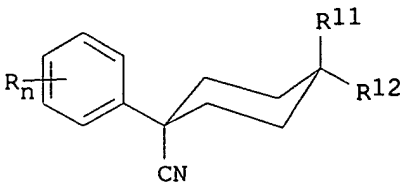


REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

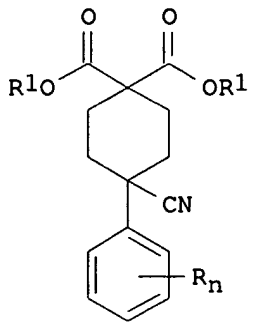
L17 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:115103 HCAPLUS
DOCUMENT NUMBER: 134:162833
TITLE: Method for preparing cyclohexanecarboxylic acids
INVENTOR(S): Diederich, Ann M.; Eldridge, Ann Marie; Mills, Robert J.; Novak, Vance J.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001010817	A1	20010215	WO 2000-US21434	20000804
W: AE, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CZ, DZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000013026	A	20020416	BR 2000-13026	20000804
EP 1200388	A1	20020502	EP 2000-952559	20000804
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
NO 2002000560	A	20020205	NO 2002-560	20020205

PRIORITY APPLN. INFO.: US 1999-147578P P 19990806
WO 2000-US21434 W 20000804
OTHER SOURCE(S): CASREACT 134:162833; MARPAT 134:162833
GI



I



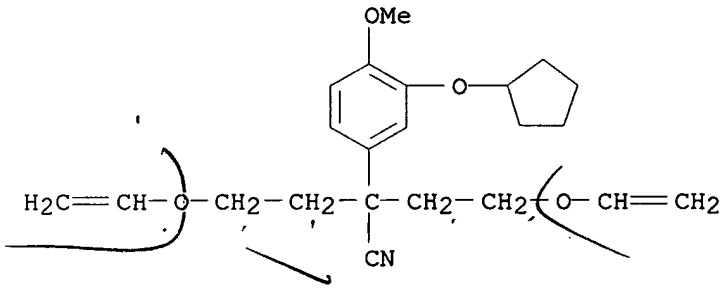
II

AB This invention relates to a method for prepg. 4-substituted-4-cyanocyclohexanecarboxylates I [R = halo, alkyl, haloalkyl, etc.; n = 1-5; R11, R12 = H, CO2X; X = H, alkyl] by forming the cyclohexane ring by treating a .alpha.,.alpha.-bis(2-haloethyl)-4-benzeneacetonitrile with a dialkyl malonate and decarboxylating the resulting diester II [R1 = H, alkyl].

IT **325767-48-4P 325767-49-5P 325767-50-8P 325767-51-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for prepg. cyclohexanecarboxylic acids)

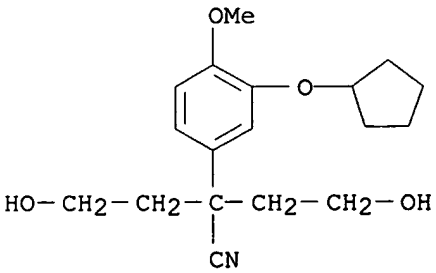
RN 325767-48-4 HCAPLUS

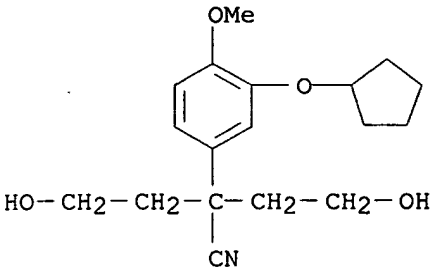
CN Benzeneacetonitrile, 3-(cyclopentyloxy)-.alpha.,.alpha.-bis[2-(ethenyloxy)ethyl]-4-methoxy- (9CI) (CA INDEX NAME)



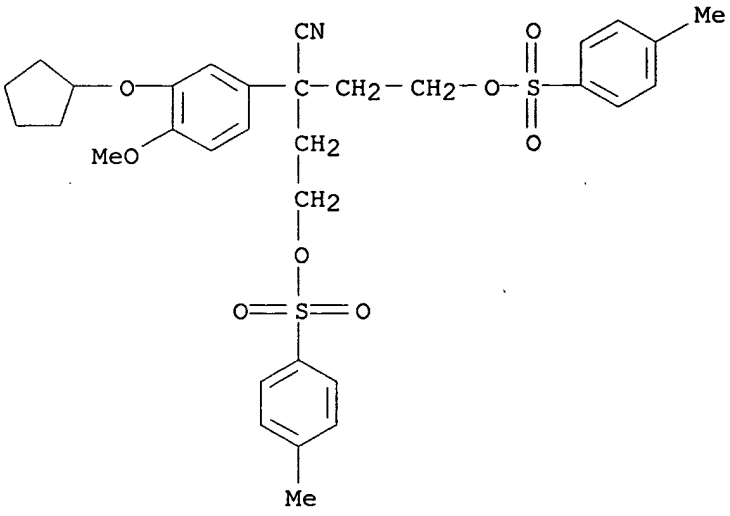
RN 325767-49-5 HCAPLUS

CN Benzeneacetonitrile, 3-(cyclopentyloxy)-.alpha.,.alpha.-bis(2-hydroxyethyl)-4-methoxy- (9CI) (CA INDEX NAME)

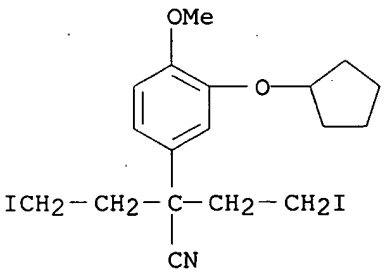




RN 325767-50-8 HCAPLUS
CN Benzeneacetonitrile, 3-(cyclopentyloxy)-4-methoxy-.alpha.,.alpha.-bis[2-[[(4-methylphenyl)sulfonyl]oxy]ethyl]- (9CI) (CA INDEX NAME)

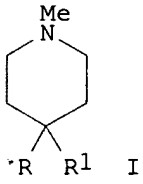


RN 325767-51-9 HCAPLUS
CN Benzeneacetonitrile, 3-(cyclopentyloxy)-.alpha.,.alpha.-bis(2-iodoethyl)-4-methoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:810810 HCAPLUS
DOCUMENT NUMBER: 132:166099
TITLE: Synthesis and dopamine and serotonin transporter binding affinities of novel analogs of meperidine
AUTHOR(S): Lomenzo, Stacey A.; Izenwasser, Sari; Gerdes, Robert M.; Katz, Jonathan L.; Kopajtic, Theresa; Trudell, Mark L.
CORPORATE SOURCE: Department of Chemistry, University of New Orleans, New Orleans, LA, 70148, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(23), 3273-3276
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

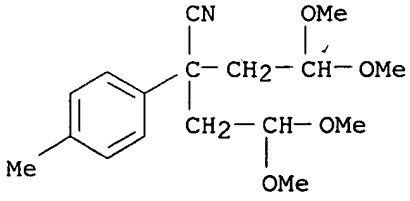


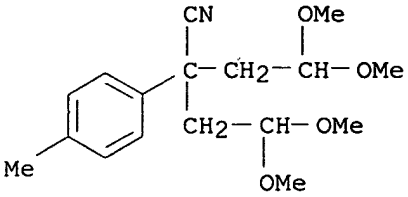
I

AB Meperidine analogs I (R = 4-substituted Ph, 3,4-dichlorophenyl, 1-naphthyl, 2-naphthyl; R1 = CN, COOEt) were prepd. and their binding affinities for the dopamine and serotonin transporters detd. The substituents on the Ph ring greatly influenced the potency and selectivity of these compds. for the transporter binding sites. In general, meperidine (I; R = Ph, R1 = COOEt) and its analogs were more selective for serotonin transporter binding sites, and the esters were more potent than the corresponding nitriles. I (R = 3,4-dichlorophenyl, R1 = COOEt) was the most potent ligand of the series for dopamine transporter binding sites while the I (R = 2-naphthyl, R1 = COOEt) exhibited the most potent binding affinity and was highly selective for serotonin transporter binding sites.

IT **258500-76-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and dopamine and serotonin transporter binding affinities of meperidine analogs)

RN 258500-76-4 HCAPLUS
CN Benzeneacetonitrile, .alpha.,.alpha.-bis(2,2-dimethoxyethyl)-4-methyl- (9CI) (CA INDEX NAME)



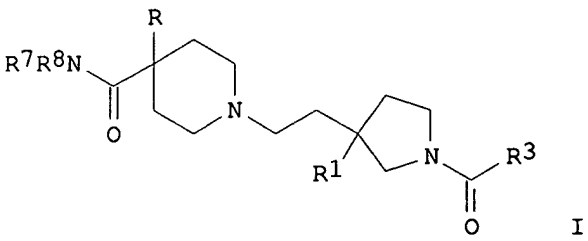


REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:56370 HCAPLUS
DOCUMENT NUMBER: 130:124994
TITLE: Preparation of 4-aryl-1-[2-(1-benzoyl-3-pyrrolidinyl)ethyl]piperidine-4-carboxamides as NK1 and NK2 receptor antagonists
INVENTOR(S): Burkholder, Timothy P.; Maynard, George D.; Kudlacz, Elizabeth M.
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA
SOURCE: U.S., 30 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5861417	A	19990119	US 1997-990672	19971215

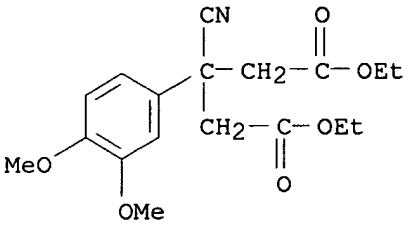
OTHER SOURCE(S): MARPAT 130:124994
GI



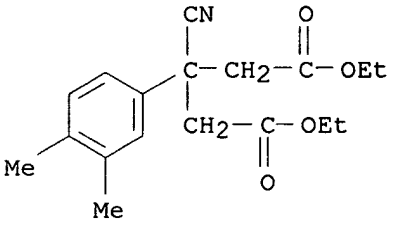
AB Title compds. [I; R = (un)substituted Ph or -pyridyl; R1 = (un)substituted Ph; R2 = ZR3; R3 = 1- or 5-tetrazolyl, 1,2,4-triazol-4-yl, etc.; R7,R8 = H; NR7R8 = piperidino, morpholino, (4-methyl)piperazino, pyrrolidino; Z = 6-(un)substituted-1,3-phenylene] were prepd. Thus, (S)-1-tert-butoxycarbonyl-3-(3,4-dichlorophenyl)-3-(2-mesyloxyethyl)pyrrolidine was aminated by 4-phenylpiperidine-4-carboxamide (prepn. each given) and the deprotected product amidated by 2-methoxy-5-(1-tetrazolyl)benzoic acid (prepn. given) to give (R)-I [R = Ph, R1 = C6H3Cl2-3,4, R2 = 2-methoxy-5-(1-tetrazolyl)phenyl, R7 = R8 = H]. Data for biol. activity of I were given.
IT **40878-20-4P**, 3-Cyano-3-(3,4-dimethoxyphenyl)-pentanedioic acid

diethyl ester **178372-09-3P**, 3-Cyano-3-(3,4-dimethylphenyl)-pentanedioic acid diethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 4-aryl-1-[2-(1-benzoyl-3-pyrrolidinyl)ethyl]piperidine-4-carboxamides as NK1 and NK2 receptor antagonists)

RN 40878-20-4 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 178372-09-3 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethylphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:689192 HCAPLUS
DOCUMENT NUMBER: 129:330656
TITLE: Preparation of 1-(3-pyrrolidinylalkyl)-4-piperidinecarboxamides as tachykinin antagonists
INVENTOR(S): Burkholder, Timothy P.; Kudlacz, Elizabeth M.; Le Tieu-bihn; Maynard, George D.
PATENT ASSIGNEE(S): Hoechst Marion Roussel Inc., USA
SOURCE: U.S., 93 pp., Cont.-in-part of U.S. 5,635,510.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

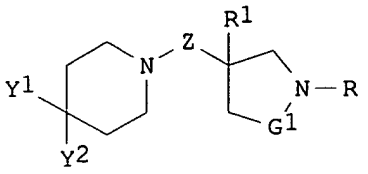
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5824690	A	19981020	US 1997-798664	19970211

ZA 9403091	A	19950112	ZA 1994-3091	19940504
US 5635510	A	19970603	US 1994-332027	19941031

PRIORITY APPLN. INFO.: US 1993-58606 B2 19930506
US 1994-225371 B2 19940419
US 1994-332027 A2 19941031

OTHER SOURCE(S): MARPAT 129:330656

GI



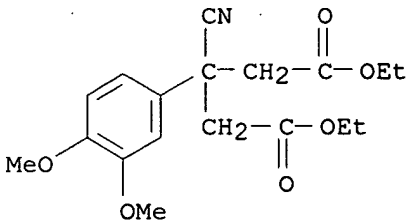
I

AB Title compds. [I; R = G2(CH2)nR2; G1,G2 = CH2 or CO; R1 = (un)substituted Ph, -naphthyl, pyridyl, etc.; R2 = (un)substituted Ph or -pyridyl; Y1 = CONHR5 or CONR6R7; R5 = H, alkyl, (CH2)qNR6R7, etc.; R6,R7 = alkyl; NR6R7 = heterocyclyl; Y2 = (un)substituted phenyl(methyl), -pyridyl, -thienyl; Y1Y2 = atoms to complete a ring; Z = (CH2)2-3; n = 0 or 1; q = 2 or 3] were prepd. Thus, 3,4-Cl2C6H3CH2CN was biscondensed with BrCH2CO2Et and the reduced product cyclized to give, after redn. and N-benzoylation, 1-benzoyl-3-(2-hydroxyethyl)-3-(3,4-dichlorophenyl)pyrrolidine. The latter was treated with MeSO2Cl and the product aminated by 4-phenylpiperidine-4-carboxamide (prepn. given) to give I (G1 = CH2, R = Bz, R1 = C6H3Cl2-3,4, Y1 = CONH2, Y2 = Ph, Z = CH2CH2). Data for biol. activity of I were given.

IT **40878-20-4P**, Diethyl 3-cyano-3-(3,4-dimethoxyphenyl)pentanedioate **167263-38-9P**, Diethyl 3-cyano-3-(3-trifluoromethylphenyl)pentanedioate **167263-64-1P 178372-09-3P**, Diethyl 3-cyano-3-(3,4-dimethylphenyl)pentanedioate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 1-(3-pyrrolidinylalkyl)-4-piperidinecarboxamides as tachykinin antagonists)

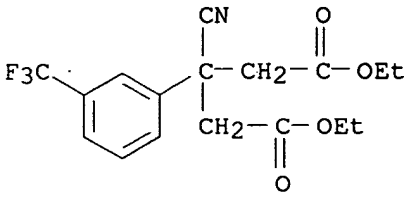
RN 40878-20-4 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)

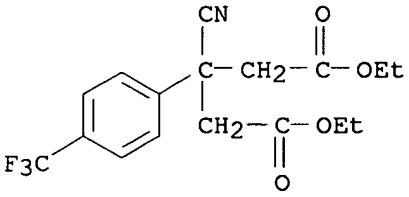


RN 167263-38-9 HCAPLUS

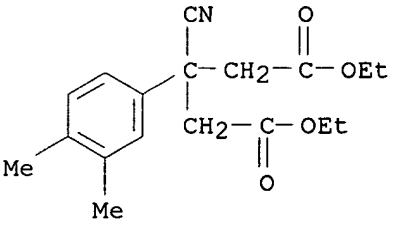
CN Pentanedioic acid, 3-cyano-3-[3-(trifluoromethyl)phenyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 167263-64-1 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-[4-(trifluoromethyl)phenyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 178372-09-3 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethylphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:424246 HCAPLUS
DOCUMENT NUMBER: 129:95499
TITLE: Novel heterocyclic substituted pyrrolidine amide derivatives useful as tachykinin receptor antagonists
INVENTOR(S): Burkholder, Thimothy P.; Maynard, George D.; Kudlacz, Elizabeth M.
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9827086 A1 19980625 WO 1997-US19884 19971103
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9851607 A1 19980715 AU 1998-51607 19971103
AU 723966 B2 20000907
EP 946548 A1 19991006 EP 1997-946443 19971103
EP 946548 B1 20020306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
CN 1241185 A 20000112 CN 1997-180825 19971103
BR 9714057 A 20000509 BR 1997-14057 19971103
JP 2001506650 T2 20010522 JP 1998-527682 19971103
AT 214063 E 20020315 AT 1997-946443 19971103
ZA 9711271 A 19980619 ZA 1997-11271 19971215
NO 9903013 A 19990818 NO 1999-3013 19990618
KR 2000057668 A 20000925 KR 1999-705496 19990618
PRIORITY APPLN. INFO.: US 1996-769812 A 19961219
WO 1997-US19884 W 19971103

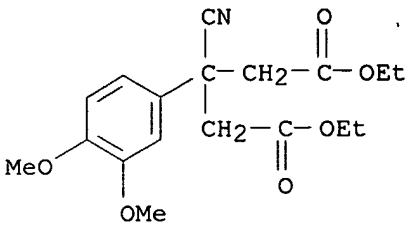
OTHER SOURCE(S): MARPAT 129:95499
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to novel heterocyclic substituted pyrrolidine amide derivs. I and stereoisomers and pharmaceutically acceptable salts thereof [wherein R1 = 1-3 of H, halo, CF3, alkyl, alkoxy; R2 = H, alkyl, alkoxy; R3 = 1-tetrazolyl or its 5-alkyl or 5-CF3 derivs., 1,2,4-triazol-4-yl; Ar = C6H4R5 or -pyridyl-R6; R5 = 1-3 of H, halo, CF3, alkyl, or alkoxy; R6 = 1-2 of H, halo, alkyl, or alkoxy; R7, R8 = H; or NR7R8 = piperidine, morpholine, piperazine, 4-methylpiperazine, or pyrrolidine ring]. As tachykinin receptor antagonists, the compds. are useful in the treatment of tachykinin-mediated diseases and conditions, including particularly asthma, cough, and bronchitis. For instance, the salt of (S)-3-(3,4-dichlorophenyl)-3-(2-hydroxyethyl)pyrrolidine with (R,R)-di-p-anisoyltartaric acid underwent a sequence of N-protection as the BOC deriv., O-mesylation, coupling of the mesylate with 4-phenylpiperidine-4-carboxylic acid amide hydrochloride, N-deprotection, amidation with 2-methoxy-5-(1H-tetrazol-1-yl)benzoic acid, and acidification, to give title compd. II as the hydrochloride. The latter bound to NK1 and NK2 receptors in vitro with IC50 values of 2.79 nM and 16.3 nM, resp. This compd. showed both higher NK1 selectivity and higher metabolic stability in comparison to a known compd. of similar structure.

IT **40878-20-4P**, 3-Cyano-3-(3,4-dimethoxyphenyl)pentanedioic acid diethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of heterocyclic substituted pyrrolidine amide derivs. as tachykinin receptor antagonists)

RN 40878-20-4 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:424245 HCAPLUS
DOCUMENT NUMBER: 129:95498
TITLE: Novel heterocyclic carboxy-substituted cyclic carboxamide derivatives useful as tachykinin receptor antagonists
INVENTOR(S): Burkholder, Timothy P.; Maynard, George D.; Kudlacz, Elisabeth M.
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA
SOURCE: PCT Int. Appl., 214 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9827085	A1	19980625	WO 1997-US21586	19971121
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5977139	A	19991102	US 1997-971891	19971117
AU 9853627	A1	19980715	AU 1998-53627	19971121
AU 718984	B2	20000504		
EP 946545	A1	19991006	EP 1997-950690	19971121
EP 946545	B1	20010905		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1240443	A	20000105	CN 1997-180774	19971121
BR 9714156	A	20000208	BR 1997-14156	19971121
AT 205200	E	20010915	AT 1997-950690	19971121
ES 2162686	T3	20020101	ES 1997-950690	19971121
JP 2002512596	T2	20020423	JP 1998-527720	19971121
ZA 9711264	A	19980623	ZA 1997-11264	19971215
NO 9903012	A	19990818	NO 1999-3012	19990618

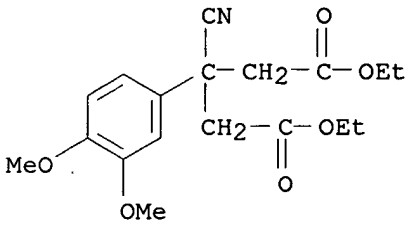
KR 2000057667 A 20000925 KR 1999-705495 19990618
PRIORITY APPLN. INFO.: US 1996-794157 A 19961219
US 1997-971891 A 19971117
WO 1997-US21586 W 19971121
OTHER SOURCE(S): MARPAT 129:95498
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to novel carboxy-substituted cyclic carboxamide derivs. I and stereoisomers and pharmaceutically acceptable salts thereof [wherein either G1 or G2 = CH2, while other = CO; m = 2 or 3; n = 0 or 1; R1 = 1-3 of H, halo, CF3, alkyl, alkoxy; R2 = 1-3 of H, halo, cyano, CF3, alkyl, alkoxy; R3 = 1-tetrazolyl or its 5-alkyl or 5-CF3 derivs., 1,2,4-triazol-4-yl, 1H-tetrazol-5-yl; Ar = (un)substituted Ph or pyridyl; A = carboxy- or carboxy-deriv.-substituted pyrrolidino, piperazino, morpholino, thiomorpholino or oxides, or piperidino]. As tachykinin receptor antagonists, the compds. are useful in the treatment of tachykinin-mediated diseases and conditions, including particularly asthma, cough, and bronchitis. For instance, (S)-3-(3,4,5-trimethoxybenzoyl)-3-(3,4-dichlorophenyl)-3-(2-methanesulfonyloxyethyl)pyrrolidine was condensed with 4-phenyl-4-[[(S)-2-carbomethoxypyrrolidin-1-yl]carboxamido]piperidine hydriodide to give title compd. II. The latter bound to NK1 and NK2 receptors in vitro with IC50 values of 4.32 nM and 4.51 nM, resp.

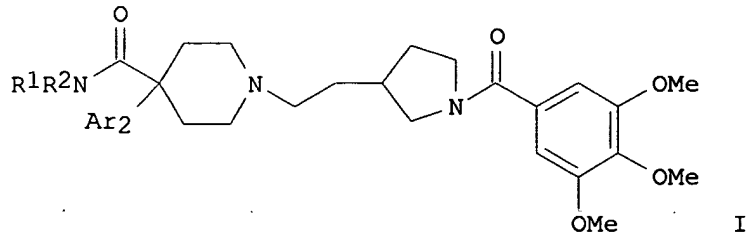
IT **40878-20-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of heterocyclic carboxy-substituted cyclic carboxamide derivs. as tachykinin receptor antagonists)

RN 40878-20-4 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:723316 HCAPLUS
DOCUMENT NUMBER: 128:34664
TITLE: Synthesis and structure-activity relationships for a series of substituted pyrrolidine NK1/NK2 receptor antagonists
AUTHOR(S): Burkholder, Timothy P.; Kudlacz, Elizabeth M.; Maynard, George D.; Liu, Xiao-Gao; Le, Tieu-Binh;

Webster, Mark E.; Horgan, Stephen W.; Wenstrup, David L.; Freund, David W.; Boyer, Fred; Bratton, Larry; Gross, Raymond S.; Knippenberg, Robert W.; Logan, Deborah E.; Jones, Bryan K.; Chen, Teng-Man; Geary, Julie L.; Correll, Melinda A.; Poole, J. Chuck; Mandagere, Arun K.; Thompson, Thomas N.; Hwang, Kin-Kai
CORPORATE SOURCE: Hoechst Marion Roussel, Cincinnati, OH, 45215, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(19), 2531-2536
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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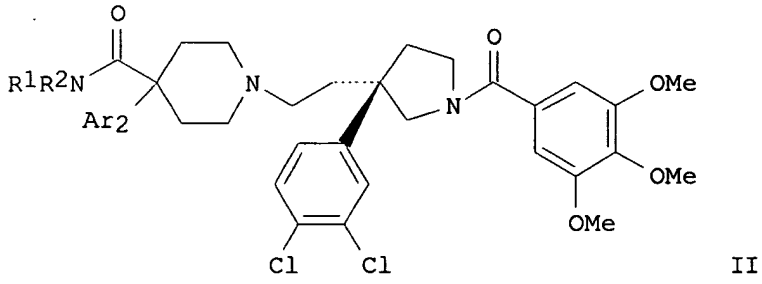


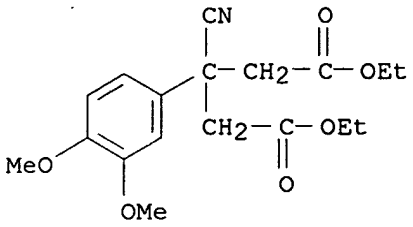
II

AB The authors recently described the synthesis and characterization of MDL 105,212, a non peptide tachykinin antagonist with high affinity for NK1 and NK2 receptors. Here, the authors report the synthesis and structure-activity relationships for a series of analogs of MDL 105,212, I (Ar1 = 3-ClC6H4, 4-FC6H4, 3-pyridyl, etc., Ar2 = Ph, 3-MeOC6H4, 4-FC6H4, 3-, 4-pyridyl, R1R2N, = H2N, piperidino, morpholino, 4-methylpiperidino) and II (Ar2 = Ph, 3-, 4-pyridyl, R1R2N = H2N, morpholino, 4-methylpiperidino), with regards to NK1 and NK2 receptor binding affinity, phys.-chem. characterization; in vitro absorption potential; in vitro metabolic stability; and efficacy in a capsaicin-challenge conscious guinea pig model after oral administration.

IT **40878-20-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and structure activity relationship of pyrrolidines as neurokinin receptor antagonists)

RN 40878-20-4 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:501538 HCAPLUS
DOCUMENT NUMBER: 127:135815
TITLE: Novel substituted 4-(1H-benzimidazol-2-yl)-[1,4]-diazepanes useful for the treatment of allergic diseases
INVENTOR(S): Kane, John M.; Maynard, George D.; Burkholder, Timothy P.; Bratton, Larry D.; Dalton, Christopher R.; Santiago, Braulio; Kudlacz, Elizabeth M.
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA
SOURCE: PCT Int. Appl., 349 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

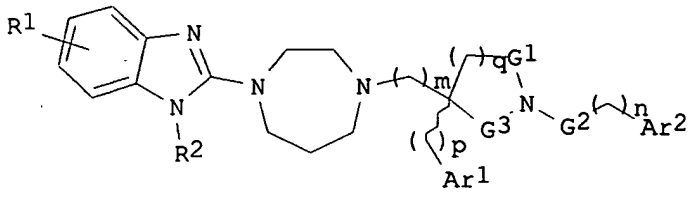
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9722604	A1	19970626	WO 1996-US19524	19961204
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2241827	AA	19970626	CA 1996-2241827	19961204
AU 9714119	A1	19970714	AU 1997-14119	19961204
AU 707914	B2	19990722		
EP 874843	A1	19981104	EP 1996-944267	19961204
EP 874843	B1	20020807		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1207097	A	19990203	CN 1996-199141	19961204
CN 1080262	B	20020306		
BR 9612074	A	19990330	BR 1996-12074	19961204
JP 2000500772	T2	20000125	JP 1997-522863	19961204
ZA 9610602	A	19970620	ZA 1996-10602	19961217
NO 9802867	A	19980819	NO 1998-2867	19980619

PRIORITY APPLN. INFO.: US 1995-580004 A 19951220

US 1996-736411 A 19961024
WO 1996-US19524 W 19961204

OTHER SOURCE(S): MARPAT 127:135815

GI



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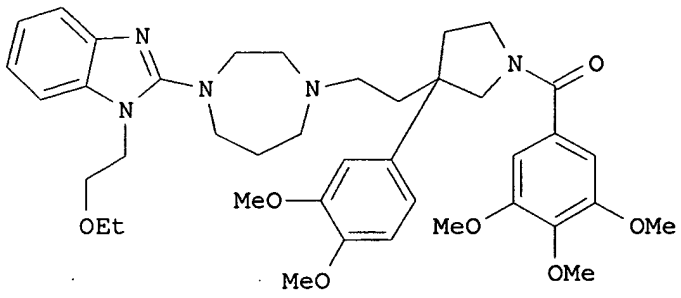


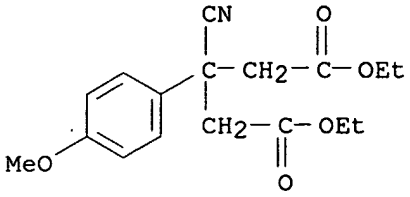
II

AB The invention relates to novel 4-(1H-benzimidazol-2-yl)-[1,4]-diazepane derivs. I and their stereoisomers and pharmaceutically acceptable salts, which are useful as histamine receptor antagonists and tachykinin receptor antagonists (no data) [wherein m = 2, 3; n = 0, 1; q = 1, 2; p = 0, 1; G1 = CH2, CO; G2 = CH2, CHMe, CO; G3 = CH2, CO; Ar1 = (un)substituted Ph, naphthyl, pyridyl, thienyl; Ar2 = (un)substituted Ph, 3,4-methylenedioxy- or 3,4-ethylenedioxyphenyl; R1 = H, halo, CF3, alkyl, alkoxy; R2 = H, certain (un)substituted alkyl or alkenyl, etc.]. Such antagonists are useful in the treatment of allergic rhinitis, including seasonal rhinitis and sinusitis, inflammatory bowel diseases, including Crohn's disease and ulcerative colitis, asthma, bronchitis, and emesis. Over 90 synthetic examples are given. For instance, 3-(3,4-dimethoxyphenyl)-3-(2-hydroxyethyl)pyrrolidine (prepn. given) underwent a sequence of amidation with 3,4,5-trimethoxybenzoyl chloride, conversion to the mesylate ester, and condensation of the mesylate with the corresponding diazepane deriv., to give title compd. II.

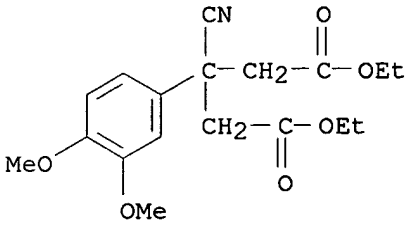
IT **40877-86-9P 40878-20-4P**, 3-Cyano-3-(3,4-dimethoxyphenyl)pentanedioic acid diethyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of benzimidazolyldiazepanes as antiallergics and antiinflammatories)

RN 40877-86-9 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 40878-20-4 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:453985 HCAPLUS
DOCUMENT NUMBER: 127:81450
TITLE: Substituted 4-(1H-benzimidazol-2-ylamino)piperidines useful for the treatment of allergic diseases
INVENTOR(S): Kane, John M.; Maynard, George D.; Burkholder, Timothy P.; Bratton, Larry D.; Dalton, Christopher R.; Santiago, Braulio; Kudlacz, Elizabeth M.
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA
SOURCE: PCT Int. Appl., 323 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719074	A1	19970529	WO 1996-US18001	19961107
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 2000500742	T2	20000125	JP 1997-517638	19961030
CA 2237971	AA	19970529	CA 1996-2237971	19961107
AU 9710508	A1	19970611	AU 1997-10508	19961107
AU 703701	B2	19990401		
CN 1202894	A	19981223	CN 1996-198360	19961107

EP 920425 A1 19990609 EP 1996-941334 19961107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
JP 11513991 T2 19991130 JP 1996-519767 19961107
IL 124396 A1 20010319 IL 1996-124396 19961107
ZA 9609484 A 19970610 ZA 1996-9484 19961112
TW 394771 B 20000621 TW 1996-85115760 19961220
NO 9802238 A 19980701 NO 1998-2238 19980515
PRIORITY APPLN. INFO.: US 1995-560419 A 19951117
US 1996-734508 A 19961017
US 1995-8108P P 19951030
US 1995-7473P P 19951122
US 1995-8992P P 19951221
US 1996-13747P P 19960320
US 1996-13748P P 19960320
US 1996-13764P P 19960320
US 1996-17455P P 19960517
US 1996-17892P P 19960517
US 1996-22047P P 19960722
US 1996-23494P P 19960907
WO 1996-US18001 W 19961107
OTHER SOURCE(S): MARPAT 127:81450

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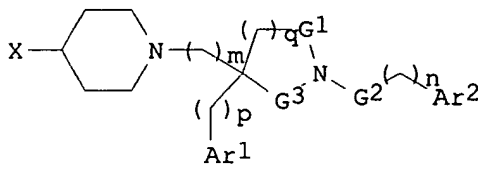

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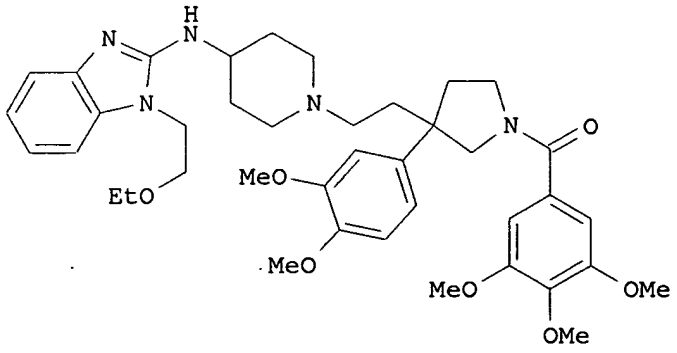


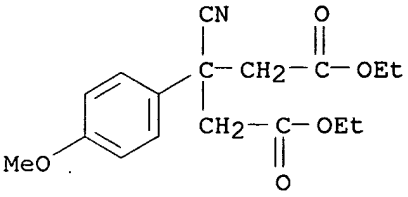
II

AB The invention relates to novel substituted piperidine derivs. I [m = 2, 3; n = 0, 1; q = 1, 2; p = 0, 1; G1 = CH2, CO; G2 = CH2, CHMe, CO; G3 = CH2, CO; Ar1 = (un)substituted Ph, naphthyl, pyridyl, or thienyl; Ar2 = (un)substituted Ph, benzodioxol-5-yl, benzodioxan-6-yl; X = (un)substituted benzimidazol-2-ylamino; with several provisos] and their stereoisomers and pharmaceutically acceptable salts. The compds. are

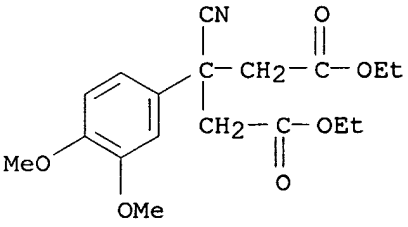
useful as histamine receptor antagonists and tachykinin receptor antagonists (no data). Such antagonists are useful in the treatment of allergic rhinitis, including seasonal rhinitis and sinusitis, inflammatory bowel diseases, including Crohn's disease and ulcerative colitis, asthma, bronchitis, and emesis. For example, 3-(3,4-dimethoxyphenyl)-3-(2-hydroxyethyl)pyrrolidine (prepn. given) underwent amidation with 3,4,5-trimethoxybenzoyl chloride, followed by mesylation with MeSO2Cl and Et3N, and coupling with [1-(2-ethoxyethyl)-1H-benzimidazol-2-yl](piperidin-4-yl)amine (prepn. given), to give title compd. II.

IT **40877-86-9P 40878-20-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of (benzimidazolylamino)piperidines as antiallergics)

RN 40877-86-9 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 40878-20-4 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2002 ACS

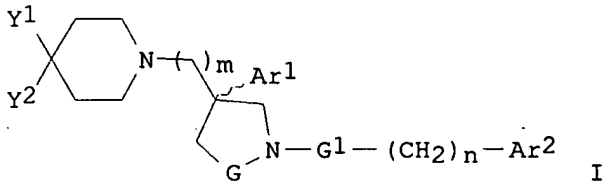
ACCESSION NUMBER:	1997:375289 HCAPLUS
DOCUMENT NUMBER:	127:95200
TITLE:	Substituted pyrrolidin-3-yl-alkyl-piperidines useful as tachykinin antagonists
INVENTOR(S):	Burkholder, Timothy P.; Kudlacz, Elizabeth M.; Maynard, George D.
PATENT ASSIGNEE(S):	Merrell Pharmaceuticals Inc., USA
SOURCE:	U.S., 82 pp., Cont.-in-part of U.S. Ser. No. 225,371, abandoned. CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5635510	A	19970603	US 1994-332027	19941031
CN 1124961	A	19960619	CN 1994-192362	19940422
CN 1081635	B	20020327		
ZA 9403091	A	19950112	ZA 1994-3091	19940504
US 5648366	A	19970715	US 1995-477167	19950607
US 5861416	A	19990119	US 1997-795576	19970206
US 5824690	A	19981020	US 1997-798664	19970211

PRIORITY APPLN. INFO.: US 1993-58606 B2 19930506
US 1994-225371 B2 19940419
US 1994-332027 A3 19941031

OTHER SOURCE(S): MARPAT 127:95200
GI



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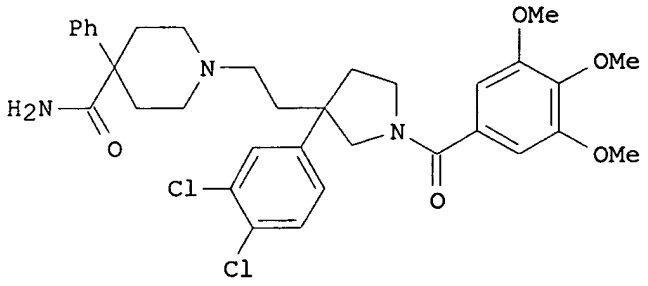


II

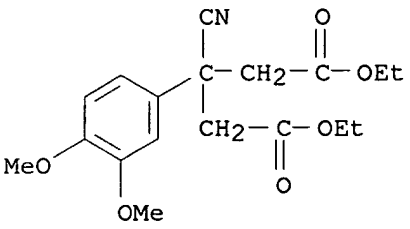
AB The invention relates to substituted pyrrolidinyl-3-yl-alkyl-piperidines I [G, G1 = CH2, CO; m = 2, 3; n = 0, 1; Ar1 = (un)substituted Ph, naphthyl, pyridyl, thienyl, or benzo[1,3]dioxan-5-yl; Ar2 = (un)substituted Ph or pyridyl; Y1 = (un)substituted CONH2; Y2 = (un)substituted Ph, naphthyl, pyridyl, thienyl, or CH2Ph; or Y1Y2 = atoms to complete certain Ph-substituted, 5-membered, diazaspiro ring fusions], their stereoisomers, N-oxides, and pharmaceutically acceptable salts, and processes for prepn. of the same. I are useful for their pharmacol. activities, such as tachykinin antagonism, and esp. substance P and neurokinin A antagonism. Such compds. are indicated for conditions assocd. with neurogenic inflammation and other diseases. For instance, 3-(3,4-dichlorophenyl)-3-(2-hydroxyethyl)pyrrolidine underwent a sequence of amidation with 3,4,5-trimethoxybenzoyl chloride (71%), conversion of the alc. to a methanesulfonate ester (92%), and reaction of the mesylate moiety with

4-phenylpiperidine-4-carboxamide-HCl (71%), to give title compd. II. In an assay for modulation of NKA-induced respiratory effects in guinea pigs, II at 10 mg/kg reduced dyspnea to 60% of control.

IT **40878-20-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of pyrrolidinylalkylpiperidines as tachykinin antagonists)

RN 40878-20-4 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



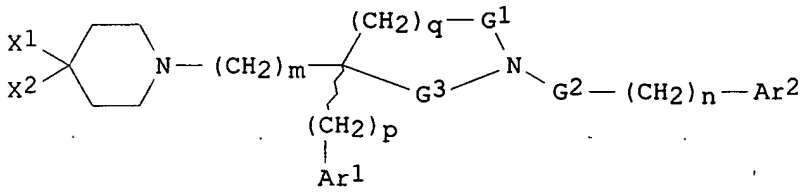
L17 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:404635 HCAPLUS
DOCUMENT NUMBER: 125:114615
TITLE: 1-Benzoyl-3-[2-[4-(1H-benzimidazole-2-carbonyl)piperidin-1-yl]ethyl]-3-phenylpyrrolidine derivatives and analogs as histamine and tachykinin receptor antagonists useful for the treatment of allergic diseases
INVENTOR(S): Burkholder, Timothy P.; Bratton, Larry D.; Kudlacz, Elizabeth M.; Maynard, George D.; Kane, John M.; Santiago, Braulio
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 294 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9606094	A1	19960229	WO 1995-US10640	19950817
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2198084	AA	19960229	CA 1995-2198084	19950817
AU 9534928	A1	19960314	AU 1995-34928	19950817
AU 693936	B2	19980709		
EP 777666	A1	19970611	EP 1995-931551	19950817

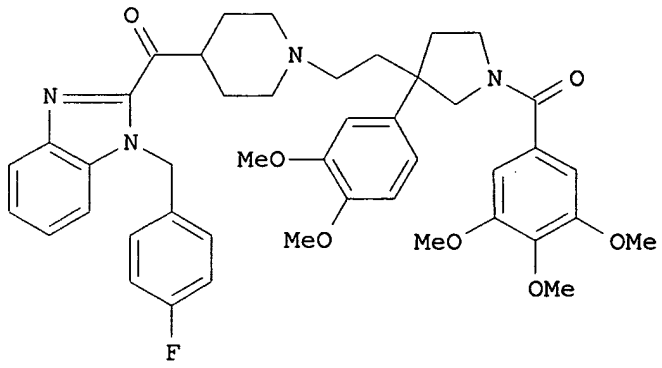
EP 777666		B1	19990303			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE						
CN 1158612		A	19970903	CN 1995-195283		19950817
CN 1067385		B	20010620			
HU 76644		A2	19971028	HU 1997-1257		19950817
JP 10504580		T2	19980506	JP 1995-508257		19950817
AT 177095		E	19990315	AT 1995-931551		19950817
ES 2132709		T3	19990816	ES 1995-931551		19950817
ZA 9507033		A	19960416	ZA 1995-7033		19950822
IL 115040		A1	20000229	IL 1995-115040		19950823
TW 430663		B	20010421	TW 1995-84108797		19950823
FI 9700771		A	19970224	FI 1997-771		19970224
NO 9700831		A	19970418	NO 1997-831		19970224
PRIORITY APPLN. INFO.:				US 1994-295960	A	19940825
				US 1995-501914	A	19950713
				WO 1995-US10640	W	19950817

OTHER SOURCE(S): MARPAT 125:114615

GI



I



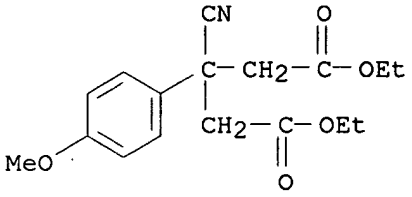
II

AB The present invention relates to novel substituted piperidine derivs. I wherein: G1 is CH2 or CO; G2 is CH2 or CO; G3 is CH2 or CO; m is 2 or 3; n is 0 or 1; q is 1 or 2; p is 0 or 1; Ar1 = (un)substituted Ph, naphthyl, pyridyl, thienyl; Ar2 = (un)substituted Ph, pyridyl; X1 and X2 are defined in one of (A), (B), or (C): (A) X1 = H and X2 = substituted benzothiazole-2-carbonyl, diphenylmethyl, benzimidazolyl-2-carbonyl; (B) X1 = OH and X2 = substituted benzothiazol-2-yl, benzimidazol-2-yl; (C) X2 = (R5C6H4)C(Z1)(C6H4R6) wherein R5, R6 = from 1 to 3 substituents chosen independently from, e.g., H, halo, CF3, and X1 and Z1 taken together form a second bond between the carbon atoms bearing X1 and Z1; provided than when G1 is CO, then G2 and G3 are CH2, and that when G2 is CO, then G1 and G3 are CH2, and that when G3 is CO, then G1 and G2 are CH2; stereoisomers thereof, and pharmaceutically acceptable salts thereof which are useful as histamine receptor antagonists and tachykinin receptor antagonists. Such

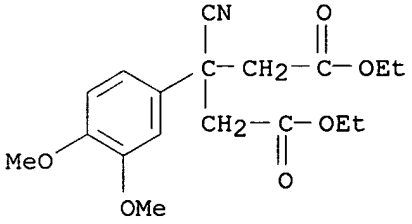
antagonists are useful in the treatment of allergic diseases including: seasonal rhinitis, allergic rhinitis, and sinusitis. Thus, e.g., substitution reaction of 4-[1-(4-fluorobenzyl)-1H-benzimidazole-2-carbonyl]piperidine with 1-(3,4,5-trimethoxybenzoyl)-3-(3,4-dimethoxyphenyl)-3-(2-methanesulfonyloxyethyl)pyrrolidine (prepn. given) afforded II which exhibited H1 receptor antagonism in vitro with pA2 = 7.50, and NK1 receptor binding affinity with IC50 = 31 nM.

IT **40877-86-9P 40878-20-4P 167263-64-1P 178370-76-8P 178372-09-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(1-benzoyl-3-[2-[4-(1H-benzimidazole-2-carbonyl)piperidin-1-yl]ethyl]-3-phenylpyrrolidine derivs. and analogs as histamine and tachykinin receptor antagonists useful for the treatment of allergic diseases)

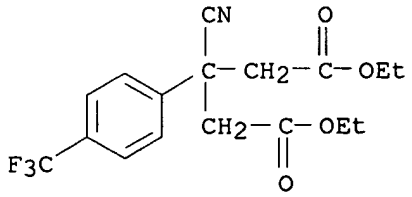
RN 40877-86-9 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



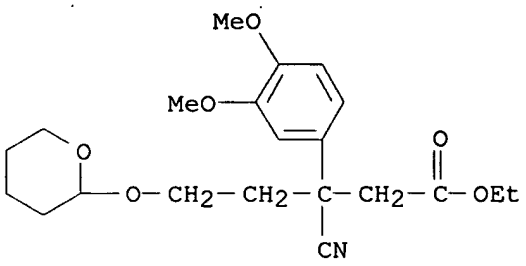
RN 40878-20-4 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



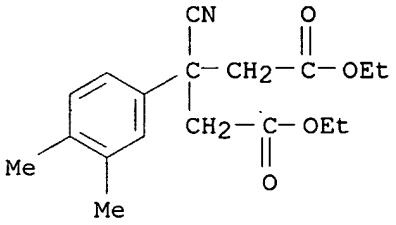
RN 167263-64-1 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-[4-(trifluoromethyl)phenyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 178370-76-8 HCAPLUS
CN Benzenepropanoic acid, .beta.-cyano-3,4-dimethoxy-.beta.-[2-[(tetrahydro-2H-pyran-2-yl)oxy]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)



RN 178372-09-3 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethylphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:772578 HCAPLUS
DOCUMENT NUMBER: 123:198629
TITLE: Preparation of substituted (pyrrolidin-3-ylalkyl)piperidines as tachykinin antagonists
INVENTOR(S): Burkholder, Timothy P.; Le, Tieu-Binh; Kudlacz, Elizabeth M.; Maynard, George D.
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 238 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9426735	A1	19941124	WO 1994-US4498	19940422
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2160462	AA	19941124	CA 1994-2160462	19940422
CA 2160462	C	19981215		

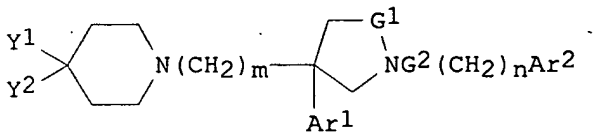
AU 9469426	A1	19941212	AU 1994-69426	19940422
AU 678023	B2	19970515		
EP 696280	A1	19960214	EP 1994-917898	19940422
EP 696280	B1	19970924		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 74085	A2	19961128	HU 1995-3153	19940422
JP 09500361	T2	19970114	JP 1994-525453	19940422
AT 158580	E	19971015	AT 1994-917898	19940422
ES 2110761	T3	19980216	ES 1994-917898	19940422
IL 109496	A1	20000726	IL 1994-109496	19940502
ZA 9403091	A	19950112	ZA 1994-3091	19940504
FI 9505258	A	19951130	FI 1995-5258	19951102
NO 9504400	A	19960108	NO 1995-4400	19951103

PRIORITY APPLN. INFO.:

US 1993-58606	A	19930506
US 1994-218483	A	19940328
US 1994-225371	A	19940419
WO 1994-US4498	W	19940422

OTHER SOURCE(S): MARPAT 123:198629

GI



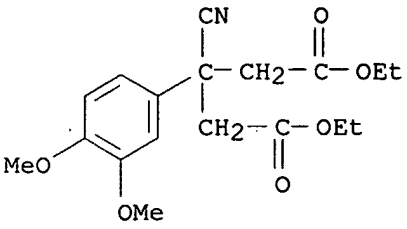
I

AB Title compds. I (G1, G2 = CH2, CO; m = 2,3; n = 0,1; Ar1, Y2 = (substituted)aryl, (substituted)heterocyclyl; Ar2 = (substituted)Ph or heterocyclyl; Y1 = (substituted)HNCO, (dialkylamino)carbonyl, N-heterocyclylcarbonyl; Y1Y2 together with the C to which they are attached form a substituted spirocyclyl), or stereoisomers, or salts thereof, are prepd. I are claimed for treatment of neurogenic inflammatory diseases, asthma, pain, and cough. 3-(3,4-Dichlorophenyl)-3-(2-hydroxyethyl)pyrrolidine (prepn. given) was reacted with 2,4-dimethoxybenzoyl chloride to give 3-(3,4-dichlorophenyl)-1-(2,4-dimethoxybenzoyl)-3-(2-hydroxyethyl)pyrrolidine which in 2 steps was converted to I (G1 = H2C, G2 = CO, m = 2, n = 0, Ar1 = 3,4-Cl2C6H3, Ar2 = 2,4-(MeO)2C6H3, Y1 = H2NCO, Y2 = Ph). Tachykinin antagonism was demonstrated.

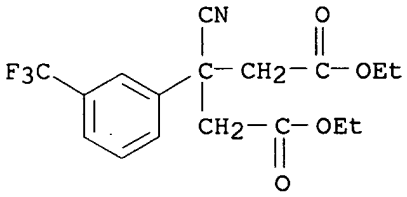
IT **40878-20-4P 167263-38-9P 167263-64-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of substituted (pyrrolidinylalkyl)piperidines as tachykinin antagonists)

RN 40878-20-4 HCAPLUS

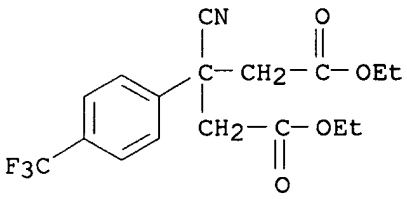
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 167263-38-9 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-[3-(trifluoromethyl)phenyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 167263-64-1 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-[4-(trifluoromethyl)phenyl]-, diethyl ester (9CI) (CA INDEX NAME)

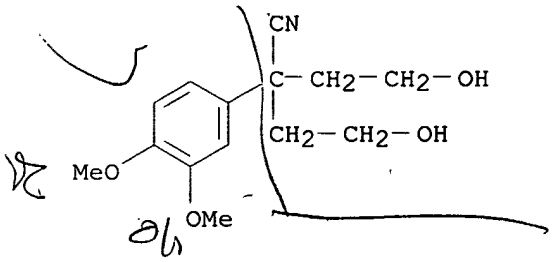


claims 10-11-12?-13?

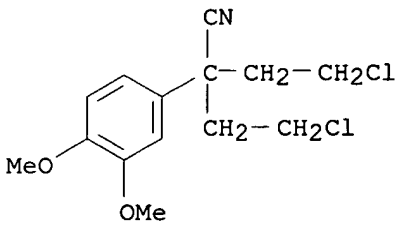
L17 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:449017 HCAPLUS
DOCUMENT NUMBER: 115:49017
TITLE: Verapamil analog with restricted molecular flexibility
AUTHOR(S): Dei, Silvia; Romanelli, M. Novella; Scapecchi, Serena; Teodori, Elisabetta; Chiarini, Alberto; Gualtieri, Fulvio
CORPORATE SOURCE: Dip. Sci. Farm., Univ. Firenze, Florence, 50121, Italy
SOURCE: J. Med. Chem. (1991), 34(7), 2219-25
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three analogs with restricted flexibility were designed to study the active conformation of verapamil during interaction with the slow calcium channel. Thus cis- and trans-1-(3,4-dimethoxyphenyl)-4-[N-[2-(3,4-dimethoxyphenyl)ethyl]-N-methylamino]-r-1-cyclohexanecarbonitrile (I and II), and 4-(3,4-dimethoxyphenyl)-N-[2-(3,4-dimethoxyphenyl)ethyl]-4-cyanopiperidine (III) in which the verapamil structure is inserted into a

cyclohexane or piperidine ring, were synthesized. Conformational anal. was performed with NMR and theor. methods, and slow calcium channel antagonism was tested on guinea pig aorta strips. The compds. are 100-times less potent than the parent compd. even if they are able to reach conformations that are quite close to the lowest energy conformation proposed for verapamil and similar compds. It appears that the flexibility to rotate around the bond between the quaternary atom and the adjacent methylene, a property which is lost in compds. I-II, is a major requisite for the calcium antagonism of verapamil.

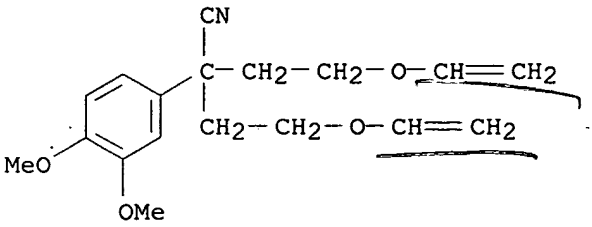
IT **133648-74-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and chlorination of)
RN 133648-74-5 HCAPLUS
CN Benzeneacetonitrile, .alpha.,.alpha.-bis(2-hydroxyethyl)-3,4-dimethoxy- (9CI) (CA INDEX NAME)



IT **133648-78-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion to cyanopiperidine deriv.)
RN 133648-78-9 HCAPLUS
CN Benzeneacetonitrile, .alpha.,.alpha.-bis(2-chloroethyl)-3,4-dimethoxy- (9CI) (CA INDEX NAME)



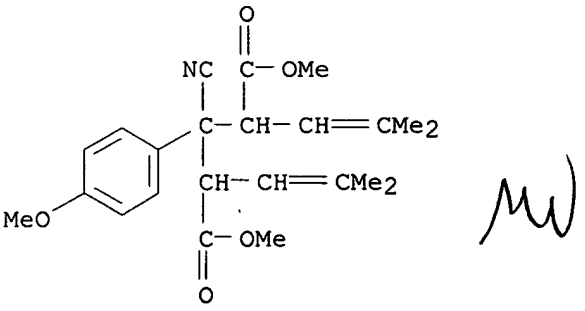
IT **133648-72-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction with chloroethyl vinyl ether)
RN 133648-72-3 HCAPLUS
CN Benzeneacetonitrile, .alpha.,.alpha.-bis[2-(ethenyloxy)ethyl]-3,4-dimethoxy- (9CI) (CA INDEX NAME)



L17 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:496775 HCAPLUS
DOCUMENT NUMBER: 113:96775
TITLE: Allylic substitution by carbon nucleophiles on 4-bromo-4-methyl-2-pentenoate: anti-Michael regioselectivity
AUTHOR(S): Roux-Schmitt, Marie Claude; Petit, Alain; Sevin, Anne; Seyden-Penne, Jacqueline; Nguyen Trong Anh
CORPORATE SOURCE: ICMO, Orsay, 91405, Fr.
SOURCE: Tetrahedron (1990), 46(4), 1263-80
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:96775

AB The reaction of carbanions .alpha. to nitriles with Me2CBrCH:CHCO2Me does not give cyclopropanes, whatever the reaction conditions, while Li enolate of Me phenylacetate does, in THF or THF-Et2O. From lithiated aminonitriles RCH(CN)NMe2 (R = substituted Ph, Ph), in THF-HMPA, the reaction leads to a mixt. of SN and SN' products in equal amts. via a radical process. From RCHR'CN (R = Ph, substituted Ph; R' = H, Me), whatever the conditions, and from Me phenylacetate enolate, either assocd. to Li in THF-HMPA or to K in THF, SN' and anti-Michael products are predominantly formed via a concerted inner sphere process, showing thus the possibility of a polar-SET mechanistic spectrum from a single electrophilic reagent.

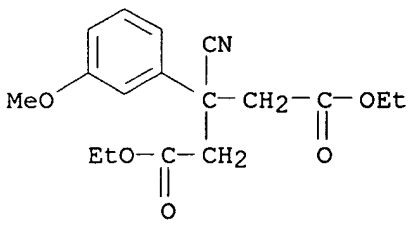
IT **128746-95-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 128746-95-2 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(4-methoxyphenyl)-2,4-bis(2-methyl-1-propenyl)-, dimethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1976:59179 HCAPLUS
DOCUMENT NUMBER: 84:59179
TITLE: Spiroindanpyrrolidine derivatives
INVENTOR(S): Bastian, Jean M.; Hasspacher, Klaus; Strasser, Michael
PATENT ASSIGNEE(S): Sandoz Ltd., Switz.
SOURCE: Swiss, 8 pp. Addn. to Swiss 556,835.
CODEN: SWXXAS
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CH 565154	A	19750815	CH 1972-9607	19720627

GI For diagram(s), see printed CA Issue.
AB The title compds. I (R1, R2, R3, R4 = H, OMe, Cl, Me) (16 compds.) were prepd. by treatment of the corresponding spiro[indan-1,3'-pyrrolidin]-3-ol (II) with 2-(3-chloropropyl)-2-(p-fluorophenyl)-1,3-dioxolane in DMF contg. Na2CO3 at 100.degree. for 20 hr followed by hydrolysis of the ketal group. II were prepd. by cyclization of the corresponding 5-oxo-3-phenyl-3-pyrrolidineacetic acid with polyphosphoric acid at 160.degree..
IT **40877-37-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 40877-37-0 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1976:59178 HCAPLUS
DOCUMENT NUMBER: 84:59178
TITLE: Spiroindanpyrrolidine derivatives
INVENTOR(S): Bastian, Jean M.; Hasspacher, Klaus; Strasser, Michael
PATENT ASSIGNEE(S): Sandoz Ltd., Switz.
SOURCE: Swiss, 8 pp. Addn. to Swiss 556,835.
CODEN: SWXXAS
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CH 565153	A	19750815	CH 1972-5483	19720413

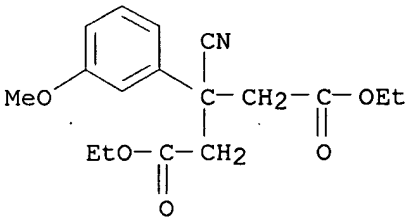
GI For diagram(s), see printed CA Issue.

AB The title compd. I (R1, R2, R3, R4 = H, Me, OMe, Cl, F, CHMe2) was prepd. by condensation of 2-(3-chloropropyl)-2-(p-fluorophenyl)-1,3-dioxolane with corresponding spiro[indan-1,3'-pyrrolidin]-3-ol which was prepd. by cyclization of the corresponding 5-oxo-3-phenyl-3-pyrrolidineacetic acid followed by redn.

IT **40877-37-0P 40877-69-8P 40877-86-9P 40877-94-9P 40878-20-4P 40878-28-2P 40878-36-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and ring closure of)

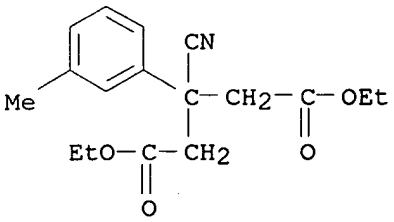
RN 40877-37-0 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



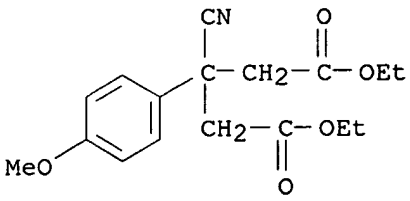
RN 40877-69-8 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3-methylphenyl)-, diethyl ester (9CI) (CA INDEX NAME)

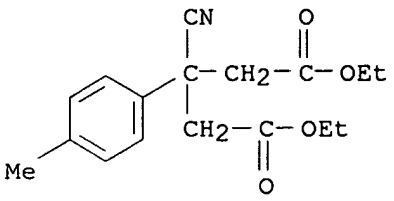


RN 40877-86-9 HCAPLUS

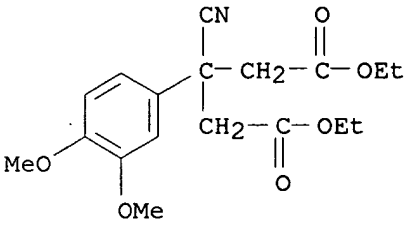
CN Pentanedioic acid, 3-cyano-3-(4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



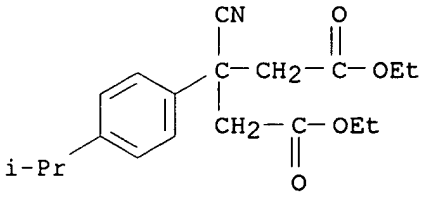
RN 40877-94-9 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(4-methylphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



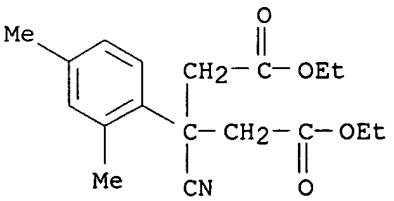
RN 40878-20-4 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 40878-28-2 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-[4-(1-methylethyl)phenyl]-, diethyl ester (9CI) (CA INDEX NAME)



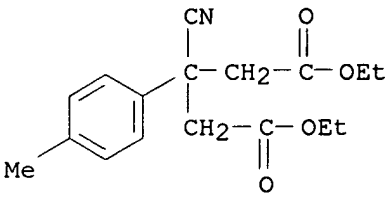
RN 40878-36-2 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(2,4-dimethylphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1976:43826 HCAPLUS
DOCUMENT NUMBER: 84:43826
TITLE: Spiroindanpyrrolidine derivatives
INVENTOR(S): Bastian, Jean M.; Hasspacher, Klaus; Strasser, Michel
PATENT ASSIGNEE(S): Sandoz Ltd., Switz.
SOURCE: Patentschrift (Switz.), 7 pp.
CODEN: SWXXAS
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CH 556837	A	19741213	CH 1973-18274	19710823

GI For diagram(s), see printed CA Issue.
AB Spiroindanpyrrolidines I (R = Ac, CONHMe, COEt, COCH2CHMe2; R1 = H, Cl, Me) were prepd. from CH2(CO2Et)2 p-R1C6H4CHO, and p-FC6H4CO(CH2)3Cl in 9 steps. I were analgesic in the tail-flick-test in mice at 1-30 mg/kg s.c. and central depressant in the climbing test in mice at 3-30 mg/kg.
IT **40877-94-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reductive cyclization of)
RN 40877-94-9 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(4-methylphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1974:146010 HCAPLUS
DOCUMENT NUMBER: 80:146010
TITLE: 1-Pyrrolidinylbutyrophenone derivatives
INVENTOR(S): Bastian, Jean M.; Strasser, Michael
PATENT ASSIGNEE(S): Sandoz Ltd.
SOURCE: Ger. Offen., 65 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2345192	A1	19740328	DE 1973-2345192	19730907
NL 7312262	A	19740313	NL 1973-12262	19730906

US 3903111	A	19750902	US 1973-394685	19730906
GB 1440380	A	19760623	GB 1973-41914	19730906
BE 804701	A1	19740311	BE 1973-135531	19730910
JP 49069661	A2	19740705	JP 1973-101293	19730910
DD 108533	C	19740920	DD 1973-173381	19730910
AU 7360170	A1	19750313	AU 1973-60170	19730910
HU 167372	P	19750927	HU 1973-SA2530	19730910
ES 418619	A1	19760601	ES 1973-418619	19730910
AT 7307802	A	19770215	AT 1973-7802	19730910
SU 548206	D	19770225	SU 1973-1957934	19730910
FR 2198756	A1	19740405	FR 1973-32612	19730911
ZA 7307236	A	19750430	ZA 1973-7236	19730911

PRIORITY APPLN. INFO.: CH 1972-13280 19720911
CH 1972-16930 19721121

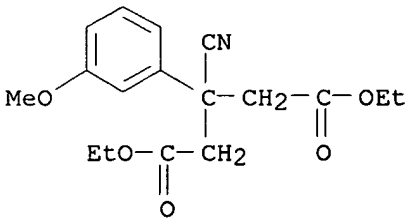
GI For diagram(s), see printed CA Issue.

AB Analgesic pyrrolidinylbutyrophenones I (R = Ph, substituted phenyl; R1 = H, Me, Et, Ac, COEt, COCMe3, CONHMe; n = 1, 2) and some related compds. (40 compds.) were prepd. Thus CH2(CO2Et)2, treated with PhCHO gave the PhCH:C(CO2Et)2 which was treated with KCN in EtOH to give NCCHPhCH2CO2Et (II). Reaction of II with BrCH2CO2Et gave NCCPh(CH2CO2Et)2 (III). Reductive cyclization of III gave Et 3-phenyl-5-oxopyrrolidine-3-acetate, which was successively hydrolyzed to the acid, reduced to the alc. with LiAlH4 and treated with Cl(CH2)3COC6H4F-p to give I (R = Ph, R1 = H, n = 2).

IT **40877-37-0P 40877-86-9P 40877-94-9P**
40878-20-4P 40878-28-2P 52424-36-9P
52424-53-0P 52424-60-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reductive cyclization of)

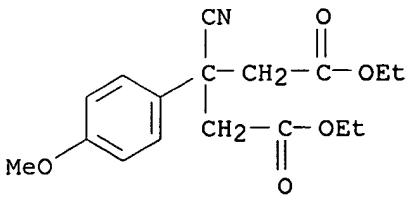
RN 40877-37-0 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 40877-86-9 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 40877-94-9 HCAPLUS
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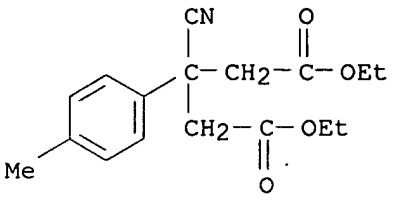
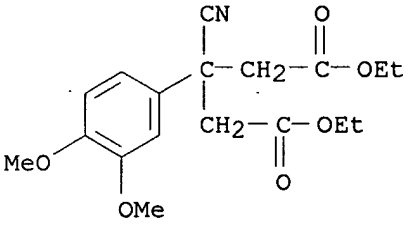
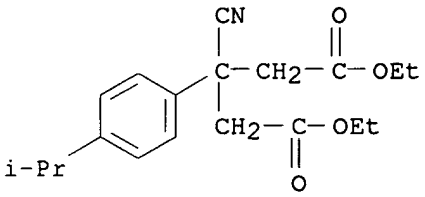


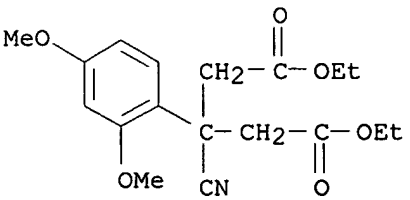
RN 40878-20-4 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



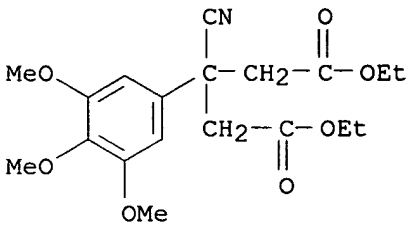
RN 40878-28-2 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-[4-(1-methylethyl)phenyl]-, diethyl ester (9CI) (CA INDEX NAME)



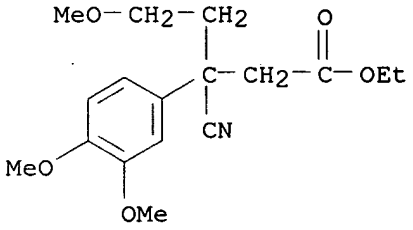
RN 52424-36-9 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(2,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 52424-53-0 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4,5-trimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 52424-60-9 HCAPLUS
CN Benzenepropanoic acid, .beta.-cyano-3,4-dimethoxy-.beta.-(2-methoxyethyl)-, ethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1973:159422 HCAPLUS
DOCUMENT NUMBER: 78:159422
TITLE: Spiro heterocyclics
INVENTOR(S): Bastian, Jean Michel; Hasspacher, Klaus; Strasser, Michael
PATENT ASSIGNEE(S): Sandoz Ltd.
SOURCE: Ger. Offen., 44 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2241027	A1	19730301	DE 1972-2241027	19720821
CH 556835	A	19741213	CH 1971-12318	19710823
ES 406008	A1	19760601	ES 1972-406008	19720421
SE 385584	B	19760712	SE 1972-10502	19720814
NL 7211304	A	19730227	NL 1972-11304	19720818
FR 2150797	A1	19730413	FR 1972-29540	19720818
BE 787804	A1	19730221	BE 1972-121173	19720821
PL 79446	P	19750630	PL 1972-157376	19720821
GB 1401048	A	19750723	GB 1972-38802	19720821
GB 1401049	A	19750723	GB 1975-4517	19720821

JP 48029765	A2	19730419	JP 1972-84027	19720822
HU 165127	P	19740628	HU 1972-SA2388	19720822
AT 7207228	A	19750915	AT 1972-7228	19720822
AT 330167	B	19760625		
DD 102146	C	19731212	DD 1972-165200	19720823
AU 7245897	A1	19740228	AU 1972-45897	19720823
ZA 7205796	A	19740424	ZA 1972-5796	19720823
ZA 7400329	A	19740529	ZA 1974-329	19720823
US 3901916	A	19750826	US 1973-419670	19731128
AT 7406072	A	19750915	AT 1974-6072	19740724

PRIORITY APPLN. INFO.:

CH 1971-12318 19710823
US 1972-282609 19720821
AT 1972-7228 19720822
CH 1972-17291 19721128

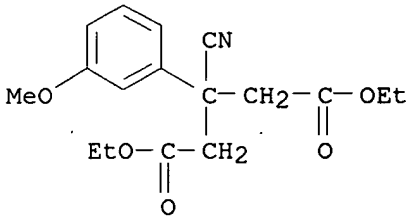
GI For diagram(s), see printed CA Issue.

AB Analgesic spiro[indan-1,3'-pyrrolidin]yl-p-fluorobutyrophenones I (R = H, R1 = H, 6-MeO, 6-Cl, 4-Cl, 5-Cl, 4-MeO, 6-Me, 5-F, 5-MeO, 5-Me, 5-Me2CH, 5,7-Cl2, 5,7-Me2, 4,5-Cl2, 5,6-(MeO)2; R = Ac, MeNHCO, EtCO, R1 = H, 5-Cl, 5-Me) were prepd. Thus, PhCHO was treated with CH2-(CO2Et)2 to give PhCH:C(CO2Et)2, which with KCN gave PhCH(CN)CH2CO2Et. The latter was treated with BrCH2CO2Et to give PhC(CN)(CH2CO2Et)2, which was cyclized with Raney Ni to Et 5-oxo-3-phenyl-3-pyrrolidinylacetate. Hydrolysis of the ester to the free acid and cyclization with polyphosphoric acid gave spiro[indan-1,3'-pyrrolidine]-3,5'-dione. LiAlH4 redn. of the ketone yielded spiro[indan-1,3'-pyrrolidin]-3-ol, which on treatment with 2-(3-chloropropyl)-2-(p-fluorophenyl)-1,3-dioxolan or Cl(CH2)3COC6H4F-p gave I (R = R1 = H).

IT **40877-37-0P 40877-69-8P 40877-86-9P**
40877-94-9P 40878-20-4P 40878-28-2P
40878-36-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 40877-37-0 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 40877-69-8 HCAPLUS

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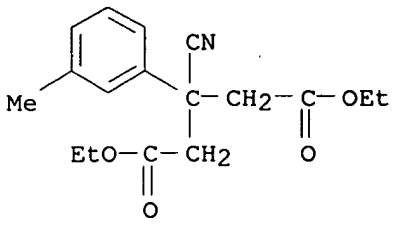
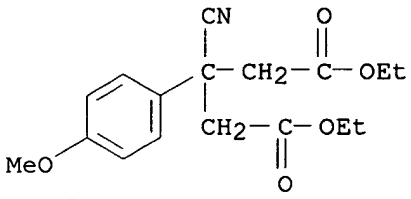
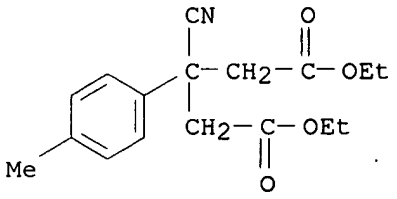


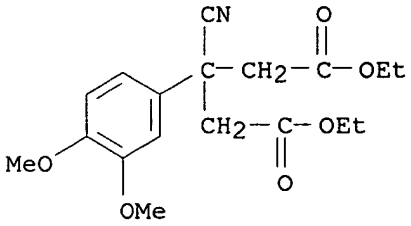
RN 40877-86-9 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(4-methoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



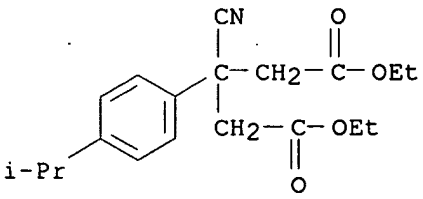
RN 40877-94-9 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(4-methylphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



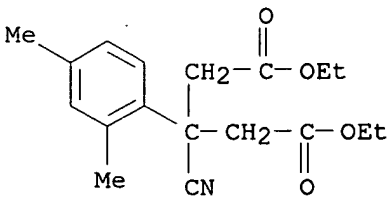
RN 40878-20-4 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(3,4-dimethoxyphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



RN 40878-28-2 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-[4-(1-methylethyl)phenyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 40878-36-2 HCAPLUS
CN Pentanedioic acid, 3-cyano-3-(2,4-dimethylphenyl)-, diethyl ester (9CI) (CA INDEX NAME)



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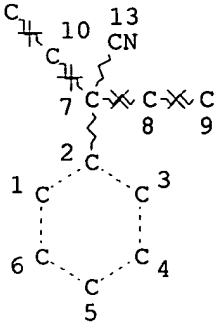

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NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE
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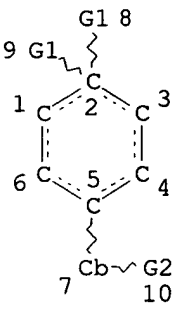
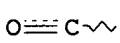


O @11  Ak @19
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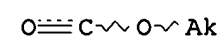
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NUMBER OF NODES IS  28

STEREO ATTRIBUTES: NONE
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L8            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7(L)PREP/RL

=> d ibib abs hitstr 1-4

L8   ANSWER 1 OF 4  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2001:115103  HCAPLUS
DOCUMENT NUMBER:          134:162833
TITLE:                    Method for preparing cyclohexanecarboxylic acids
INVENTOR(S):              Diederich, Ann M.; Eldridge, Ann Marie; Mills, Robert
                          J.; Novak, Vance J.
PATENT ASSIGNEE(S):       Smithkline Beecham Corporation, USA
SOURCE:                   PCT Int. Appl., 19 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
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     WO 2001010817      A1   20010215      WO 2000-US21434  20000804
         W:  AE, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CZ, DZ, EE, GE, GH, GM,
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             MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA,
             US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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PRIORITY APPLN. INFO.:                  US 1999-147578P  P  19990806
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OTHER SOURCE(S):          CASREACT 134:162833; MARPAT 134:162833
GI
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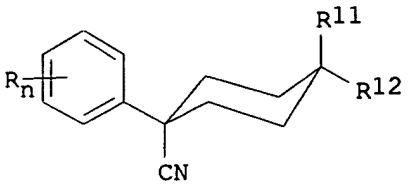

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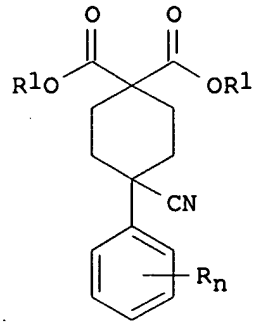


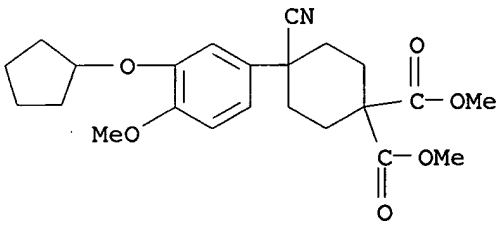
II

AB This invention relates to a method for prepg. 4-substituted-4-cyanocyclohexanecarboxylates I [R = halo, alkyl, haloalkyl, etc.; n = 1-5; R11, R12 = H, CO2X; X = H, alkyl] by forming the cyclohexane ring by treating a .alpha.,.alpha.-bis(2-haloethyl)-4-benzeneacetonitrile with a dialkyl malonate and decarboxylating the resulting diester II [R1 = H, alkyl].

IT **325767-52-0P 325767-53-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(method for prepg. cyclohexanecarboxylic acids)

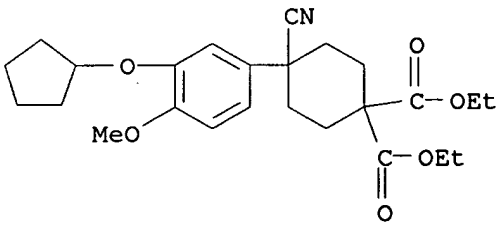
RN 325767-52-0 HCAPLUS

CN 1,1-Cyclohexanedicarboxylic acid, 4-cyano-4-[3-(cyclopentyloxy)-4-methoxyphenyl]-, dimethyl ester (9CI) (CA INDEX NAME)



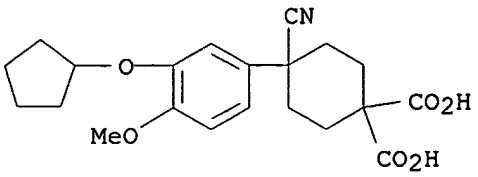
RN 325767-53-1 HCAPLUS

CN 1,1-Cyclohexanedicarboxylic acid, 4-cyano-4-[3-(cyclopentyloxy)-4-methoxyphenyl]-, diethyl ester (9CI) (CA INDEX NAME)



IT **325767-54-2P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(method for prepg. cyclohexanecarboxylic acids)

RN 325767-54-2 HCAPLUS
CN 1,1-Cyclohexanedicarboxylic acid, 4-cyano-4-[3-(cyclopentyloxy)-4-methoxyphenyl]- (9CI) (CA INDEX NAME)



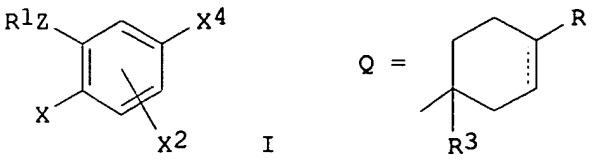
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

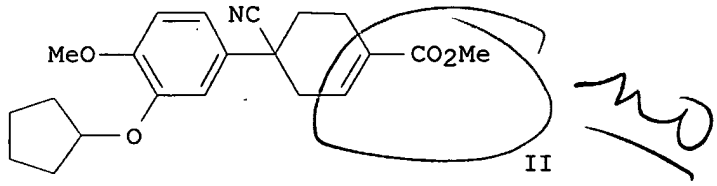
L8 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:128097 HCAPLUS
DOCUMENT NUMBER: 126:211907
TITLE: Preparation of phenylcyclohexanecarboxylates as antiallergics and antiinflammatories
INVENTOR(S): Christensen, Siegfried B., IV
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: U.S., 17 pp., Cont.-in-part of U.S. Ser. No. 968,762, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5602157	A	19970211	US 1995-443641	19950518
HU 70523	A2	19951030	HU 1994-2817	19930305
CZ 283425	B6	19980415	CZ 1994-2397	19930305
EP 919544	A1	19990602	EP 1998-204466	19930305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
ES 2157923	T3	20010901	ES 1993-907233	19930305
ZA 9302264	A	19931015	ZA 1993-2264	19930330
AU 9733229	A1	19971023	AU 1997-33229	19970808
AU 705566	B2	19990527		
AU 9936759	A1	19990819	AU 1999-36759	19990624
AU 724115	B2	20000914		

PRIORITY APPLN. INFO.:
US 1992-862030 B2 19920402
US 1992-968762 B2 19921030
EP 1993-907233 A3 19930305
SG 1996-7903 A 19930305
AU 1997-33229 A3 19970808

OTHER SOURCE(S): MARPAT 126:211907
GI





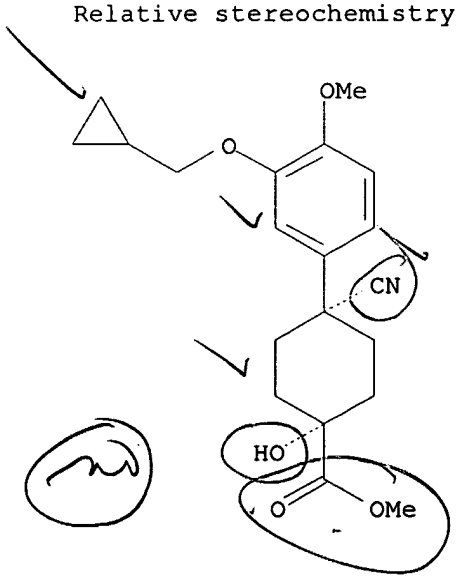
AB Title compds. [I; R1 = (CR4R5)nZ1(CR4R5)mR6; R4,R5 = H or alkyl; R6 = H, OH, Me, cycloalkyl, aryl, etc.; X = halo, NR4R5, YR2; R2 = (halo)methyl or -ethyl; X3 = H or groups cited for X; X4 = e.g., cyclohex(en)yl group Q; R = CO2H, alkoxycarbonyl, cyano, CONH2, etc.; R3 = H, halo, alkyl, cyano, NH2, etc.; Z = O or (alkyl)imino; Z1 = CO2, CONR4, or O, m = 0-2, and n = 1-4 or Z1 = bond, n = 0 and m = 1-6; dashed line = optional bond] were prepd. as phosphodiesterase IV and tumor necrosis factor inhibitors (no data). Thus, 4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)cyclohexanone was converted to the enol trifluoromethanesulfonate and the latter methoxycarbonylated to give title compd. II.

IT **153259-87-1P 153259-88-2P 153259-93-9P 153259-95-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(prepn. of phenylcyclohexanecarboxylates as antiallergics and antiinflammatories)

RN 153259-87-1 HCAPLUS

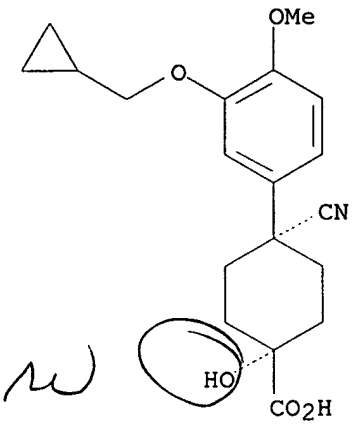
CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopropylmethoxy)-4-methoxyphenyl]-1-hydroxy-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



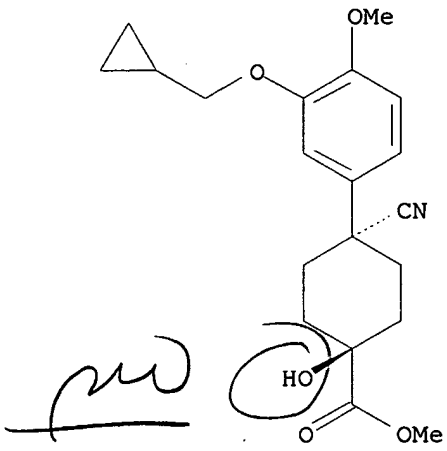
RN 153259-88-2 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopropylmethoxy)-4-methoxyphenyl]-1-hydroxy-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



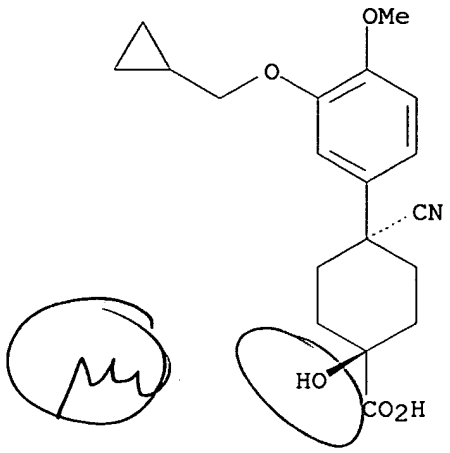
RN 153259-93-9 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopropylmethoxy)-4-methoxyphenyl]-1-hydroxy-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 153259-95-1 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopropylmethoxy)-4-methoxyphenyl]-1-hydroxy-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



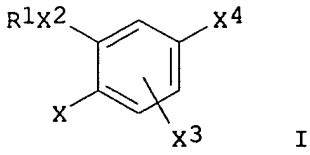
L8 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:563635 HCAPLUS
DOCUMENT NUMBER: 125:275885
TITLE: Preparation of benzene derivatives useful for treating allergic and inflammatory diseases
INVENTOR(S): Christensen, Siegfried B., IV
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: U.S., 18 pp., Cont.-in-part of U. S. Ser. No. 968,762, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5552438	A	19960903	US 1994-313094	19940929
WO 9319749	A1	19931014	WO 1993-US1991	19930305
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, RO, RU, SD, SE, SK, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
CZ 283425	B6	19980415	CZ 1994-2397	19930305
EP 919544	A1	19990602	EP 1998-204466	19930305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
ZA 9302264	A	19931015	ZA 1993-2264	19930330
US 5614540	A	19970325	US 1995-457942	19950518
US 5643946	A	19970701	US 1995-443636	19950518
AU 9936759	A1	19990819	AU 1999-36759	19990624
AU 724115	B2	20000914		

PRIORITY APPLN. INFO.:
US 1992-862030 B2 19920402
US 1992-968762 B2 19921030
WO 1993-US1991 W 19930305
EP 1993-907233 A3 19930305
SG 1996-7903 A 19930305
US 1994-313094 A1 19940929
AU 1997-33229 A3 19970808

OTHER SOURCE(S): MARPAT 125:275885

GI



I

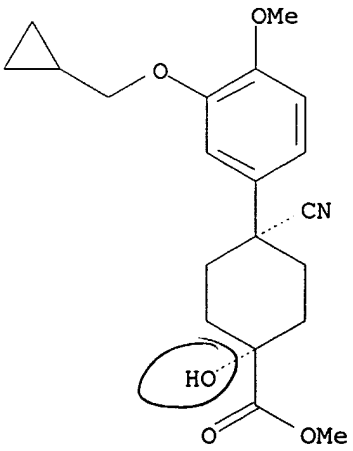
AB The title compds. [I; R1 = (un)substituted carboxyalkyl derivs., (un)substituted aminocarbonylalkyl derivs., (un)substituted alkyl, etc.; X = halogen, NO2, (un)substituted NH2, formyl amine (sic), MeO, EtO, etc.; X2 = O, (un)substituted NH; X3 = H, X; X4 = substituted cyclohexyl or cyclohexenyl], useful for inhibiting the prodn. of tumor necrosis factor (no data) and in the mediation or inhibition of the enzymic or catalytic activity of phosphodiesterase IV (no data), are prepd. Thus, cis-[1-[2-cyanoethyl]-5-[4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)cyclohexyl]tetrazole] was reacted with aq. NaOH in THF/H2O and the mixt. acidified with HCl, producing cis-[4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)-1-(5-tetrazolyl)cyclohexane], m.p. 190-191.degree..

IT **153259-87-1P 153259-88-2P 153259-93-9P 153259-95-1P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(prepn. of benzene derivs. useful for treating allergic and inflammatory diseases)

RN 153259-87-1 HCAPLUS

CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopropylmethoxy)-4-methoxyphenyl]-1-hydroxy-, methyl ester, cis- (9CI) (CA INDEX NAME)

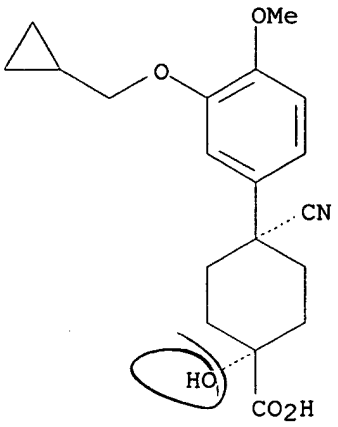
Relative stereochemistry.



RN 153259-88-2 HCAPLUS

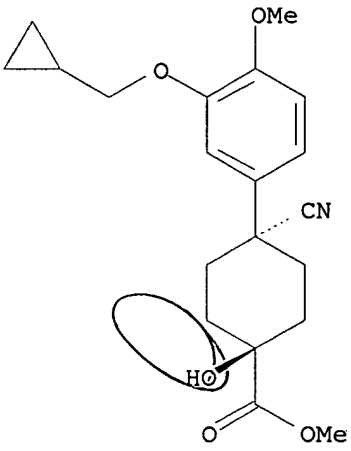
CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopropylmethoxy)-4-methoxyphenyl]-1-hydroxy-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



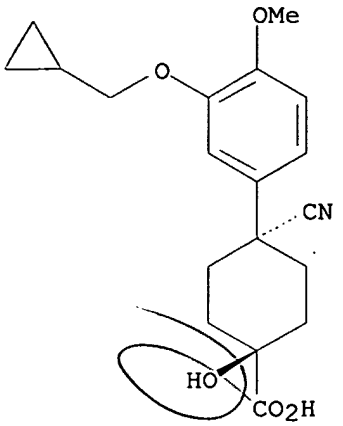
RN 153259-93-9 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopropylmethoxy)-4-methoxyphenyl]-1-hydroxy-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 153259-95-1 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopropylmethoxy)-4-methoxyphenyl]-1-hydroxy-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L8 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:244186 HCAPLUS
DOCUMENT NUMBER: 120:244186
TITLE: Preparation of arylcyclohexanecarboxylates useful for treating allergic and inflammatory diseases
INVENTOR(S): Christensen, Siegfried B., IV
PATENT ASSIGNEE(S): SmithKline Beckman Corp., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9319749	A1	19931014	WO 1993-US1991	19930305
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, RO, RU, SD, SE, SK, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9337910	A1	19931108	AU 1993-37910	19930305
AU 677776	B2	19970508		
EP 633776	A1	19950118	EP 1993-907233	19930305
EP 633776	B1	20010509		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07508508	T2	19950921	JP 1993-517446	19930305
JP 2873090	B2	19990324		
HU 70523	A2	19951030	HU 1994-2817	19930305
PL 172857	B1	19971231	PL 1993-305614	19930305
CZ 283425	B6	19980415	CZ 1994-2397	19930305
PL 173963	B1	19980529	PL 1993-317029	19930305
EP 919544	A1	19990602	EP 1998-204466	19930305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
SK 279958	B6	19990611	SK 1994-1171	19930305
RU 2136656	C1	19990910	RU 1994-45291	19930305
RO 115872	B1	20000728	RO 1994-1601	19930305
AT 200980	E	20010515	AT 1993-907233	19930305
ES 2157923	T3	20010901	ES 1993-907233	19930305

ZA 9302264	A	19931015	ZA 1993-2264	19930330
IL 105221	A1	20000131	IL 1993-105221	19930330
CN 1092406	A	19940921	CN 1993-105725	19930402
CN 1066436	B	20010530		
US 5552438	A	19960903	US 1994-313094	19940929
NO 9403663	A	19941115	NO 1994-3663	19940930
FI 9404549	A	19941130	FI 1994-4549	19940930
AU 9733229	A1	19971023	AU 1997-33229	19970808
AU 705566	B2	19990527		
AU 9936759	A1	19990819	AU 1999-36759	19990624
AU 724115	B2	20000914		

PRIORITY APPLN. INFO.:

US 1992-862030	A2	19920402
US 1992-968762	A2	19921030
EP 1993-907233	A3	19930305
SG 1996-7903	A	19930305
WO 1993-US1991	A	19930305
AU 1997-33229	A3	19970808

OTHER SOURCE(S): MARPAT 120:244186

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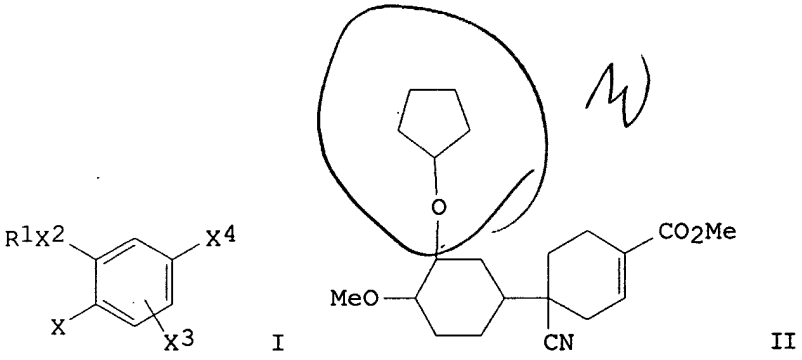


I II

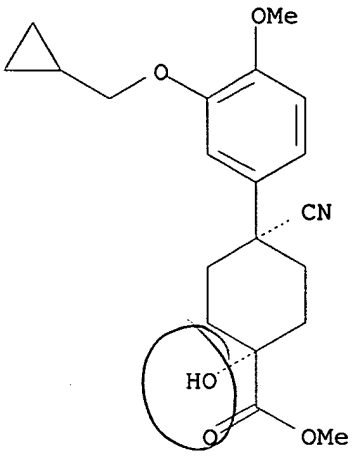
AB Title compds. I [R1 = R6(R5R4C)mO2C(R5R4C)n, R6(CR4R5)mNCO(R5R4C)n, R6(R5R4C)r wherein R6 = H, Me, HO, (halo)aryl, (halo) aryloxy-C1-3-alkyl, C3-6 cycloalkyl, etc., R4, R5 = H, (substituted) C1-2 alkyl, m = 0-2; n = 1-4, r = 1-6; X = halo, O2N, R5R4N, R2Y, wherein R2 = (halo) Me or Et, Y = O, S(O)m' wherein m' = m; X2 = O, R8N wherein R8 = H, (fluoro-C1-4) alkyl; X3 = H, X; X4 = (substituted) cyclohyxenyl or cyclohexyl] or a salt thereof, useful for treatment of allergic and inflammatory disease, and inhibition of tumor necrosis factor and phosphodiesterase IV inhibitors (no data), are prepd. To Me2CH02NH in THF was added 4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)cyclohexan-1-one to give 4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)-1-cyclohexenyl trifluoromethylsulfonate which was treated with Pd(Ph3P)4 to give title II.

IT **153259-87-1P 153259-88-2P 153259-93-9P**
153259-95-1P
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of, for treatment of allergic and inflammatory diseases)

RN 153259-87-1 HCAPLUS

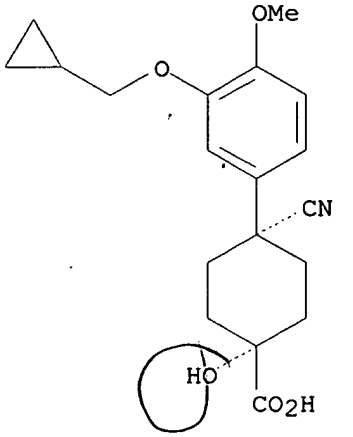
CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopropylmethoxy)-4-methoxyphenyl]-1-hydroxy-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



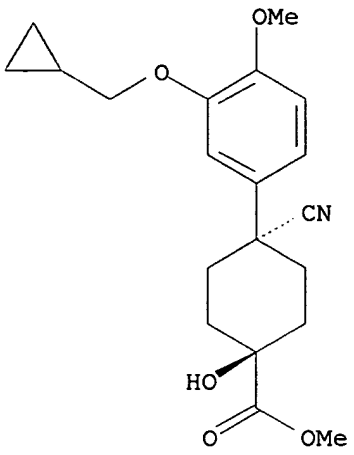
RN 153259-88-2 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopropylmethoxy)-4-methoxyphenyl]-1-hydroxy-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 153259-93-9 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopropylmethoxy)-4-methoxyphenyl]-1-hydroxy-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 153259-95-1 HCAPLUS
CN Cyclohexanecarboxylic acid, 4-cyano-4-[3-(cyclopropylmethoxy)-4-methoxyphenyl]-1-hydroxy-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.